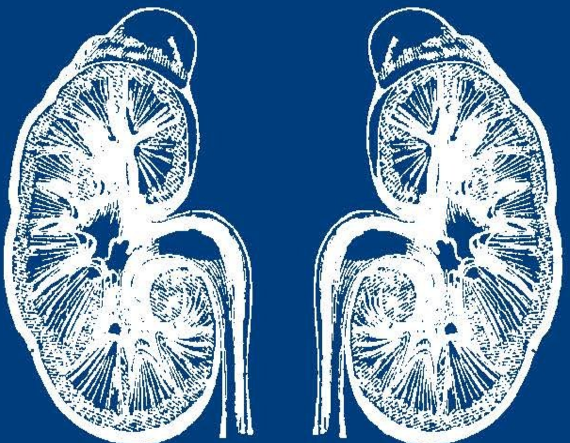
4th Edition

Choe's Urology Oral Board Self-Assessment



Editor
Lawrence L. Yeung, MD

Anadem Publishing

CHOE'S UROLOGY ORAL BOARD SELF-ASSESSMENT
4TH EDITION

BY JONG M. CHOE, MD

EDITOR, Lawrence L. Yeung, MD

CONTRIBUTORS

Jeremy Bergamo, MD
Aaron Brafman, MD
Peter Cai, MD
Benjamin K. Canales, MD, MPH
Bilal I. Chughtai, MD
Paul L. Crispen, MD
Romano T. DeMarco, MD
Gregory J. Diorio, DO
Scott M. Gilbert, MD
Mohit Gupta, MD
Julia Han, MD
Samay Jain, MD
Nikki P. Le, MD
Andrew R. Leone, MD
James Bradley Mason, MD
John P. Mulhall, MD, MSc, FECSM, FACS
Bobby B. Najari, MD
Brandon Otto, MD
Sijo J. Parekattil, MD
Jonathan Pavlinec, MD
Edward N. Rampersaud, MD
Philippe E. Spiess, MD
Dominique Thomas, BS
Marla Wardenburg, MD
Akira Yamamoto, MD
Uwais B. Zaid, MD
Anja Zann, MD

Anadem Publishing, Inc.
3620 North High Street
Columbus, OH 43214
800-633-0055 / 614-262-2539 / Fax: 614-262-6630
anadem@anadem.com / www.anadem.com

Using This Book

This book is based upon information from sources believed to be reliable. In developing this book the publisher, author, contributors, reviewers and editors have made substantial efforts to make sure that the regimens, drugs and treatments are correct and are in accordance with currently accepted standards. The material in this book is presented to professionals for educational and informational purposes and is not meant to be, and should not relied upon for, recommendations regarding diagnosis or treatment for any actual cases. Further, in compiling a resource such as this there is the possibility of human error. The publisher, author, contributors, reviewers and editors do not guarantee success on any examination and disclaim any liability, loss or damage as a result, directly or indirectly, from using or applying any of the contents of this book.

Copyright © 2017 by the Estate of Jong M. Choe. All rights reserved, including translation. This book is protected by copyright. No part of this book may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, or by any information storage or retrieval system without prior written permission from the copyright owner.

ISBN: 978-1-890018-80-1

TABLE OF CONTENTS

1. Diseases of the Adrenal Gland 1
2. Bladder Carcinoma 19
3. Upper Tract Urothelial Carcinoma 59
4. Penile Carcinoma 73
5. Prostate Carcinoma 89
6. Renal Cell Carcinoma 115
7. Testicular Cancer 149
8. Infectious Diseases 183
9. Stone Disease 207
10. Female Urology 235
11. Voiding Dysfunction 247
12. Male Infertility 291
13. Sexual Dysfunction 309
14. Pediatrics 339
15. Renal Transplantation 379
16. Urologic Problems of Pregnancy 391
17. Urethral Obstruction 399
18. Urologic Trauma 415
19. Urethral Strictures 439

CHAPTER 1

DISEASES OF THE ADRENAL GLAND

MOHIT GUPTA, MD
PAUL CRISPEN, MD

CASE 1

HPI: 45-year-old Caucasian female who has been referred for evaluation of an incidentally found 2 cm right adrenal lesion on a non-contrast CT abdomen/pelvis. On evaluation, the patient is hypertensive despite being started on multiple medications in the last year. Review of systems is notable for worsening lethargy, an unintentional 20 pound weight gain over the past four months, and excessive facial hair. The patient had her last menses two weeks ago and is not pregnant. She denies steroid use. Review of the patient's non-contrast CT scan demonstrates a 2 cm right adrenal lesion with an attenuation of 22 Hounsfield units (HU).

PMH: HTN, impaired fasting glucose

PSH: none

Allergies: NKDA

Medications: Lisinopril, Metoprolol, Amlodipine, HCTZ, Metformin

FH: (-) cardiac disease or hypertension
SH: (+) tob, 1 PPD × 10 years; (-) ETOH; patient is a pharmacist
ROS: as per above; review of all other 14 systems negative

PE:

Vitals	T 98.6	BP 170/110	P 90	RR 12
GA	CF in no apparent distress			
HEENT	moon facies; excessive facial hair			
Heart	RRR			
Lungs	no increased work of breathing on room air			
Spine	(+) Buffalo hump			
Abdomen	obese; soft, non-tender/non-distended, (+) abdominal striae			
Flank	(-) CVAT			
Pelvic	normal female			
Rectal	benign			
Ext	(-) cyanosis; (-) clubbing; (-) edema			
Neuro	ambulates without assistance and has no gross neurologic abnormalities			

What initial lab tests do you order?

UA → WNL
Chem 7 → Na 135 meq/L; K 3.2 meq/L; Cl 100 meq/L; CO2 24 meq/L; BUN 10 mg/dL; Cr 1.0 mg/dL
CBC → WNL
Pregnancy test → negative

What is your differential diagnosis?

Pheochromocytoma, Conn's syndrome, renal artery stenosis, Cushing's syndrome, and non-functional adrenal adenoma.

What kinds of screening lab tests do you order now?

1. Serum metanephrines → normal
2. Serum renin and aldosterone → normal
3. Low dose dexamethasone suppression test → abnormal (positive)

When evaluating for Cushing's syndrome, 3 tests are available—24-hour urinary free cortisol (UFC) evaluation, an overnight low-dose (1 mg) dexamethasone suppression test and the late-night salivary cortisol test.

The low dose dexamethasone suppression test and the late night salivary cortisol test are the preferred screening tests, especially for the evaluation of incidental adrenal masses.

Measurement of plasma-free metanephrines and normetanephrines is indicated for evaluation of pheochromocytoma given the patient's history of significant hypertension. Alternatively, 24-hr fractionated urinary metanephrines may be measured.

Determining the ratio of plasma aldosterone concentration (PAC) to plasma renin activity is utilized to evaluate for primary aldosteronism, which is indicated given the patient's history of significant hypertension.

How is a low-dose dexamethasone suppression test performed?

The overnight 1 mg dexamethasone suppression test is performed by administration of 1 mg of dexamethasone at 11 PM and determination of a fasting plasma cortisol level the following morning at 8 AM. A positive dexamethasone test (persistently elevated cortisol) confirms that the patient has Cushing's syndrome.

What lab would you obtain at this point?

Serum ACTH: not elevated

What are causes of Cushing's syndrome?

Potential causes of Cushing's syndrome can be categorized into ACTH dependent versus independent etiologies.

ACTH-dependent etiologies include excessive secretion of ACTH by the pituitary gland (Cushing's syndrome) (70%), ectopic ACTH production by non-pituitary tumors (10–15%), and ectopic production of corticotropin-releasing hormone (<1%) (such as bronchial carcinoma).

ACTH-independent etiologies include cortisol-secreting adenomas of the adrenal gland or adrenal carcinoma (10%).

What is your assessment?

45-year-old CF with Cushing's syndrome and a functional 2 cm right adrenal lesion.

What would you have done if the patient had an elevated serum ACTH?

1. Obtain head CT or MRI
2. Inferior petrosal vein sampling for ACTH
   a. This is the gold standard for establishing the diagnosis of Cushing's syndrome as a significant proportion of patients with Cushing's syndrome will have a normal CT or MRI
   b. Neurosurgery consult if patient has evidence of pituitary tumor or elevated ACTH on petrosal vein sampling
3. Trans-sphenoidal hypophysectomy: surgery of choice for pituitary adenoma

How would you manage this functional adenoma?

Patients with unilateral cortisol-secreting adrenal masses are treated with ipsilateral adrenalectomy.

You perform a successful open adrenalectomy without complication. Overnight, however, the patient becomes confused, nauseous, hypotensive, and tachycardic with incomplete response from fluid boluses.

What should you be concerned for?

Excess cortisol secretion from the patient's functional adenoma may have caused suppression of her normal HPA axis. As a result, the production of ACTH by the pituitary and the remaining adrenal gland have been suppressed and the patient is in severe acute adrenocortical insufficiency.

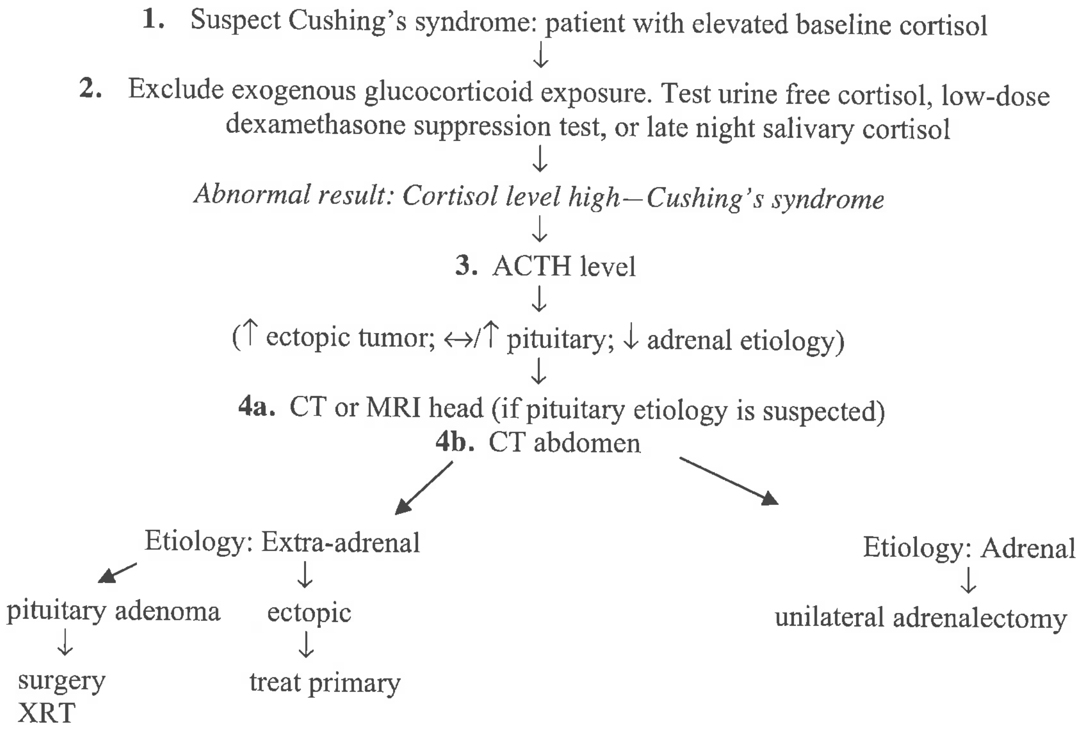
In addition to aggressive volume replacement therapy, how would you manage this patient?

Administer glucocorticoid replacement with hydrocortisone 100 mg intravenously or dexamethasone 4 mg intravenously. Mineralocorticoid replacement is not necessary in an acute setting.

What is subclinical Cushing's syndrome?

Subclinical Cushing's syndrome is hypercortisolism without the signs and symptoms of Cushing's syndrome. It is typically diagnosed during the evaluation of incidental adrenal masses and detection is increasing with routine functional evaluations.

Flow Chart for Cushing's syndrome:


1. Suspect Cushing's syndrome: patient with elevated baseline cortisol
2. Exclude exogenous glucocorticoid exposure. Test urine free cortisol, low-dose dexamethasone suppression test, or late night salivary cortisol
Abnormal result: Cortisol level high—Cushing's syndrome
3. ACTH level
(↑ ectopic tumor; ↔/↑ pituitary; ↓ adrenal etiology)
4a. CT or MRI head (if pituitary etiology is suspected)
4b. CT abdomen
Etiology: Extra-adrenal
pituitary adenoma
surgery
XRT
ectopic
treat primary
Etiology: Adrenal
unilateral adrenalectomy

How do you treat incidental adrenal masses?

Biochemically active → Unilateral, functionally active incidentalomas should be surgically removed irrespective of size in acceptable surgical candidates

Biochemically inactive → The risk of adrenocortical carcinoma increases with the size of the mass. Therefore:

< 4 cm → If the mass is not biochemically active, repeat imaging with CT or MRI at 3–6 months and then annually for 1–2 years. Hormonal evaluation should be annually for up to 5 years. Should the tumor grow more than 1 cm or become hormonally active during follow-up, surgical excision should be considered

> 4 cm → Solid mass: surgical removal should be considered due to risk of malignancy

CASE 2

HPI: 55-year-old Caucasian male who has been referred to the clinic for evaluation of an incidental right adrenal mass found on CT abdomen/pelvis with oral contrast performed in the emergency room for abdominal pain and nausea. The patient's symptoms have resolved and he is asymptomatic at the time of his clinic visit. Review of the CT imaging demonstrates a 3 cm right, irregular adrenal mass with calcifications and an attenuation of 35 HU. No intravenous contrast imaging is available.

PMH: HTN, COPD, obstructive sleep apnea, BPH

PSH: none

Allergies: none **Medications:** Flomax, Lisinopril, HCTZ, Metoprolol

FH: (-) GU malignancies
SH: (+) tob, 20 pack year; (+) ETOH, 2 beers nightly
ROS: non-contributory

PE:

Vitals	T 98.6	BP 140/60	P 90	RR 12
GA	CM in no apparent distress			
Heart	RRR			
Lungs	no increased work of breathing on room air, clear to auscultation bilaterally			
Abdomen	obese; soft, non-tender/non-distended			
Flank	(-) CVAT			
Rectal	25 g prostate without nodularity			
Ext	(-) cyanosis; (-) clubbing; (-) edema			
Neuro	ambulates without assistance and has no gross neurologic abnormalities			

Lab work from the ER:

UA → WNL
Chem 7 → Na 135 meq/L; K 3.6 meq/L; Cl 100 meq/L; CO2 27 meq/L; BUN 10 mg/dL; Cr 1.3 mg/dL
CBC → WNL
PT/PTT → WNL

The patient's primary care physician obtained the following lab-work prior to referring the patient to your clinic:

Low-dose dexamethasone suppression test → normal
Plasma metanephrines → normal
Aldosterone → normal
Renin → normal

What other studies could you obtain to help establish the diagnosis in this patient?

1. CT scan with intravenous contrast washout study: 3 cm right irregular adrenal mass with calcifications with 20% washout

2. MRI: the mass appears isointense relative to the liver or spleen on T1-weighted images and demonstrates intermediate to increased intensity on T2-weighted images
3. Sexual steroids and steroid precursors: 17-OH-progesterone, DHEA-S (17B-estradiol and testosterone only need to be evaluated in the case of feminization or virilization)

What imaging characteristics help differentiate a benign adrenal lesion from a malignant one?

1. An adrenal adenoma can be identified by measuring enhancement and contrast-washout on CT
    a. Lesions that have an attenuation value below 10 HU on non-contrast CT scan are adenomas
    b. After intravenous administration of a contrast agent, benign adrenal lesions will commonly wash out more than 50% on the delayed scan, whereas lesions such as metastatic tumors, carcinomas, or pheochromocytomas demonstrate <50% washout
2. Alternatively, a non-contrast MRI may be utilized to evaluate signal intensity between in phase and out of phase imaging
    a. Adrenal masses which demonstrate loss of signal intensity on out of phase sequences are considered adenomas

What is your next step?

Complete staging to rule out metastatic disease: obtain a CXR or CT scan of the chest.

There is no evidence of metastatic disease.

What is your assessment?

55-year-old CM with a 3 cm adrenal mass concerning for localized adrenocortical carcinoma.

How would you manage this mass?

Complete surgical excision is essential in the management of adrenal cortical carcinomas and offers the best chance of cure and control of symptoms related to the tumor should the lesion be functionally active. En bloc resection of surrounding organs involved with locally advanced disease should be performed whenever possible.

State that you would obtain an informed consent, preoperative lab work, and provide the patient with appropriate preoperative antibiotics and thrombosis prophylaxis. A nasogastric or orogastric tube can be placed to decompress the bowel, especially helpful for transperitoneal cases. The placement of a urinary catheter to help measure urine output and to decompress the bladder is essential.

Note: When embarking on renal or adrenal surgery, the contralateral adrenal gland must be evaluated. Corticosteroid therapy is not necessary for patients undergoing unilateral adrenalectomy with a normal contralateral adrenal gland. However, when CT scan shows contralateral adrenal atrophy or agenesis, supplemental corticosteroids may be required before, during, and after unilateral adrenalectomy.

You re-reviewed the CT scan. Films showed a normal-appearing contralateral adrenal gland.

Note: Severe coagulopathy and poor cardiopulmonary performance status are absolute contraindications to adrenalectomy.

Discuss your surgical technique:

The Operation (Radical Adrenalectomy)

1. Anterior subcostal, Chevron, flank retroperitoneal, or thoracoabdominal approach
2. Open Gerota's fascia and dissect surrounding tissues away from the adrenal gland
3. Minimal manipulation of adrenal mass/ "No touch technique"
4. Ligate or clip adrenal arteries
5. Ligate adrenal vein
6. Inspect the adrenal fossa for bleeding
7. Perform regional node dissection
8. Drains are not necessary
9. Deliver the specimen (via specimen removal bag if laparoscopic) and close the incision

What is the blood supply of the adrenal gland?

The blood supply of the adrenal artery is composed of inferior phrenic artery, aorta, and renal artery.

What are alternative approaches?

The role of laparoscopy in treating malignant adrenal masses is not established.

Experienced laparoscopic surgeons may approach tumors suspicious for adrenocortical carcinoma with caution as these tumors are usually large, may be locally invasive, and the only chance of cure for these patients is complete surgical resection.

Smaller, radiographically organ-confined disease can be approached laparoscopically but must be performed with caution due to the risk of tumor spillage.

Discuss potential complications of adrenal surgery and their management.

1. During the clamping of adrenal vein, patient becomes hypotensive
    a. This is normal response to clamping of adrenal vein
    b. Simply replacing volume with normal saline will restore the BP
    c. Pressors are rarely needed
2. During dissection, adrenal vein is avulsed from IVC
    a. First, digital compression
    b. Clear the field of blood
    c. Proximal and distal control with sponge sticks
    d. Oversew the hole with 4-0 Prolene
3. During dissection, IVC is lacerated
    a. Proximal and distal control with sponge sticks
    b. Satinsky or Allis clamp to oppose the caval edges
    c. Oversew the injury with 4-0 Prolene
4. During the operation, pleural leak is seen
    a. Insert a Robinson catheter into the pleural injury
    b. Place purse-string suture using 3-0 chromic suture around the Robinson catheter
    c. The air from the pleura is evacuated either by suction on the catheter or by placing the catheter under water seal

   d. Using negative pressure, the tube is quickly removed, and the purse-string is simultaneously tied
5. After the operation, pneumothorax is noted on CXR
   a. If pneumothorax is >15%, chest tube should be placed
   b. If pneumothorax is <15% and patients are not in respiratory distress and do not have mediastinal shift, they may be followed expectantly with supplemental nasal O2
6. During the operation, splenic injury is noted
   a. For small tears of the splenic capsule, the area may be fulgurated with electrocautery or Argon beam laser. This is reinforced with thrombin-soaked Gelfoam. Fibrin glue may be used as well
   b. Minor laceration of the spleen may be managed with Surgicel and Avitene
   c. Moderate splenic lacerations should be closed with bolsters of Surgicel in addition to Avitene
   d. Severe lacerations mandate splenectomy
      i. Splenectomy is performed by dividing the short gastric vessels followed by division of splenic artery and vein
      ii. Patients who have undergone splenectomy should receive Pneumovax therapy and should be given prophylactic penicillin for dental work
7. During the operation, duodenal injury is suspected
   a. Duodenal lacerations should be repaired in multiple layers with interrupted sutures
      i. Use 4-0 silk for the serosa
      ii. Place omental wrap and insert NGT for bowel rest
   b. Duodenal hematomas should be observed
      i. If hematomas expand and increase in size, they should be opened to identify and control the bleeding site
      ii. After the bleeding is controlled, the serosa is closed using 4-0 silk and omentum is placed on the closure
8. During dissection, the pancreas is injured
   a. If the pancreatic duct is not injured, parenchymal laceration should be repaired by closing the pancreatic capsule with non-absorbable sutures
   b. All pancreatic tears (with or without duct injury) should be treated with abdominal drain
   c. Injuries involving distal tail of the pancreas with ductal injuries should be managed by resection of the distal portion of the pancreas with a suture ligation of the duct and closure of the pancreatic capsule
      i. Do not re-anastomose the transected duct since you risk significant complications. If this occurs in your protocol, ask for general surgery consult, but your examiner may have given him a day off so be prepared to discuss this
   d. Treatment of pancreatic fistula involves long-term TPN until spontaneous healing has occurred. Surgical closure is rarely necessary
9. During dissection, the liver is lacerated
   a. Liver lacerations may be repaired with horizontal mattress sutures using a Surgicel bolster
   b. Deep lacerations of the liver with bile leak should be drained
   c. If significant bleeding occurs from liver injury, hemorrhage may be controlled with Pringle maneuver (cross clamping of the porta hepatis) until patient is stable
   d. If partial hepatectomy is necessary, call for general surgeon

He tolerates the operation and is admitted to the floor in stable condition.

What is your follow-up?

Check pathology of the specimen and serum chemistries.

Pathology: metastatic (node positive) adrenal carcinoma
Chem 7: normal

During surveillance, your patient is noted to have metastatic progression imaging studies.

How do you manage metastatic adrenal carcinoma?

Combination therapy of Mitotane, Etoposide, Doxorubicin, and Cisplatin.

Unfortunately, the majority of patients with adrenal cortical carcinomas present with advanced disease, and treatment of ACC often includes multimodal therapy. Treatment options are limited. Whenever possible, patients should be referred for participation in a clinical trial.

Follow-up should include CT examination of the chest, abdomen, and pelvis every 3 months for the first 2 years. The value of routine PET imaging in disease surveillance has not been established.

Mitotane is an oral synthetic derivative of the insecticide dichlorodiphenyltrichloroethane (DDT) and has demonstrated clinical benefit in the adjuvant setting following surgical resection and in patients with metastatic disease. Currently, it remains the primary systemic therapy, either as a single agent or in combination with other cytotoxic drugs.

As a single agent, overall responses to Mitotane range from 14% to 36%, with few studies demonstrating a significant survival benefit. Daily doses of 10–12 grams are necessary and GI and neurological side effects are usually dose-limiting.

Due to the adrenolytic effect of Mitotane, steroid replacement is typically necessary during therapy. Recent trials have demonstrated a response rate of 36% with the combination of Mitotane and Streptozotocin, and a response rate of 49% with the combination of Mitotane, Etoposide, Doxorubicin, and Cisplatin.

Enrollment into a clinical trial should be considered in most patients given the high rate of local recurrence and metastatic progression despite complete surgical resection.

How does adrenal carcinoma typically present clinically?

Patients may have mixed clinical syndromes such as virilization, feminization, and uncontrolled hypertension.

Approximately 50–79% are functionally active. Most commonly, hypercortisolism (30–50%), androgen excess (20%), estrogen excess (10%), and rarely aldosteronism (2–5%). On physical examination, affected patients may have a palpable abdominal mass due to the large average size, >10cm, of adrenocortical carcinomas.

CASE 3

HPI: 50-year-old Caucasian female with uncontrolled hypertension, despite being started on at least 3 medications by her primary care physician. She endorses chronic headache and intermittent chest palpitations. Recent cardiac evaluation in the ER for chest pain was negative.

PMH: Hypertension, hyperlipidemia, asthma (mild), (-) CAD, (-) PVD

PSH: none

Allergies: none **Medications:** Hytrin, Metoprolol, Amlodipine, Lipitor

FH: (-) adrenal disease
SH: (-) tob; (-) ETOH
ROS: (+) bilateral lower extremity weakness, (+) intermittent headaches

PE:

Vitals	T 98.6 BP 170/100 P 75 RR 12
GA	calm
HEENT	(-) papilledema; (-) AV nicking; (-) carotid bruits
Heart	RRR
Lungs	no increased work of breathing on room air; clear to auscultation bilaterally
Abdomen	soft; non-tender, non-distended; no abdominal bruits
Flank	benign
Bimanual pelvic	normal female
Ext	(-) cyanosis; (-) clubbing; (-) edema
Neuro	ambulates without assistance; no gross neurologic abnormalities

What initial lab tests do you order?

UA → normal
CBC → WNL
Chem 7 → K 2.5 meq/L; CO2 38 meq/L; BUN 10 mg/dL; Cr 1.2 mg/dL
EKG → normal
hCG → negative

What is your initial assessment?

This patient has evidence of hypertension with metabolic alkalosis and hypokalemia.

What is your differential diagnosis?

Differential diagnosis includes Conn's syndrome, Cushing's syndrome, pheochromocytoma, essential hypertension, and renovascular hypertension.

Her history of hypertension and hypokalemia is most consistent with primary hyperaldosteronism (Conn's syndrome). You want to work her up for hyperaldosteronism or aldosterone-producing adenoma (APA). However, normokalemia does not exclude hyperaldosteronism since 70–90% of patients with Conn's syndrome in contemporary series will have normal potassium levels at diagnosis.

What are the first diagnostic tests you would order?

Screen for adrenal source of hypertension.

Plasma metanephrines:

1. Low dose dexamethasone suppression test
2. Plasma aldosterone to renin ratio

Obtain AM plasma renin activity (PRA): → Low
Obtain AM plasma aldosterone activity (PAC): → Elevated
PAC:PRA ratio: → 35

Prior to initiating screening, hypokalemia should be corrected and all mineralocorticoid receptor antagonists should be stopped at least 6 weeks prior to testing. Patients requiring these agents for control of severe hypertension should be transitioned to agents such as α_1-receptor blockers or long-acting calcium channel blockers.

If plasma renin level was high, what would it mean?

A high plasma renin activity level may indicate renin-mediated hypertension pathophysiology such as renal artery stenosis (RAS), cirrhosis, heart failure, or reninoma/juxtaglomerular cell tumor.

What is your next step?

Perform a confirmatory test to secure the diagnosis of primary aldosteronism. 1 of 4 tests can be performed:

1. Intravenous saline infusion test (preferred)
2. Oral sodium loading test
3. Captopril suppression test
4. Fludrocortisone suppression test (less commonly used)

Saline suppression test: serum aldosterone 21 ng/dL (normal < 10 ng/dL)

How is a saline suppression test performed?

1. Saline suppression tests are performed with the patient in supine position
2. 2 liters of IV saline is infused over 4 hours and serum aldosterone is measured
3. The infusion is performed in the morning after an overnight fast

Following the infusion, a plasma aldosterone concentration of greater than 5 ng/dL is diagnostic of primary aldosteronism.

What happens to normal patients during saline infusion?

In normal individuals, saline infusion increases the blood pressure, resulting in inhibition of renin-angiotensin-aldosterone pathway. Thus, normal individuals will demonstrate decreased renin and aldosterone levels in response to saline suppression test.

What happens to patients with aldosterone producing adenoma during saline infusion?

Patients with aldosterone producing adenoma will have low baseline renin level. In response to saline suppression test, these individuals will continue to demonstrate a high aldosterone levels (often greater than 10 ng/dL) and decreased renin levels.

In this case, failure to suppress aldosterone level suggests aldosteronoma.

What do you do now?

Following the diagnosis of primary aldosteronism, subtype differentiation is indicated. Begin by obtaining an adrenal CT scan to evaluate for the presence of adrenal nodules.

CT scan: normal bilateral adrenal glands

Note: Approximately 20% of aldosterone-producing adenomas may be less than 1 cm.

What is the next step?

Obtain adrenal vein sampling.

By establishing lateralization, various subtypes of primary aldosteronism can be differentiated and patients in which adrenalectomy is potentially beneficial can be identified.

How is this performed?

1. After an overnight fast, an adrenal vein sampling is performed by obtaining percutaneous access to the femoral vein
   a. Catheter tips are positioned to obtain blood samples from the left adrenal vein, right adrenal vein, and the inferior vena cava
   b. These samples are analyzed for aldosterone and cortisol concentrations
2. Appropriate specimen collection from the adrenal vein is determined by comparing the cortisol concentrations from the adrenal vein samples to the cortisol concentration from the IVC sample, which should be less
3. If specimen collection is correct, lateralization of aldosterone secretion is determined by comparing the aldosterone to cortisol ratios of the dominant to non-dominant sides
   a. Aldosterone secretion is considered to be lateralized if the ratio is greater than 2:1
4. The routine use of ACTH stimulation during adrenal vein sampling is controversial

Note: Adrenal vein sampling of aldosterone remains the cornerstone for localization of aldosterone production. Imaging studies such at CT and MRI alone cannot accurately delineate lateralization of aldosterone hypersecretion.

Adrenal vein sampling in this patient did not demonstrate lateralization of aldosterone secretion.

What is your assessment?

Non-lateralizing primary aldosteronism consistent with bilateral adrenal hyperplasia.

How would you manage this patient?

1. Medical therapy with aldosterone receptor antagonists, such as spironolactone and eplerenone, is indicated for this patient
2. Other antihypertensive medications as well as several lifestyle changes, including weight loss, a low-sodium diet, and exercise regimens will often be needed
3. Surgical therapy is not appropriate treatment for bilateral adrenal hyperplasia

What are complications of aldosterone receptor antagonists?

Side effects include gynecomastia, impotence, menstrual disturbances, and hyperkalemia. Eplerenone may provide a more favorable side-effect profile compared to spironolactone.

When is surgical management of primary aldosteronism recommended?

Surgically correctable subtypes of primary aldosteronism:

1. Aldosterone producing adenoma
2. Primary unilateral adrenal hyperplasia
3. Ovarian aldosterone-secreting tumor
4. Aldosterone-producing carcinoma

Non-surgically correctable subtypes of primary aldosteronism:

1. Bilateral adrenal hyperplasia
2. Familial hyperaldosteronism types I–III

How is aldosterone secretion regulated?

1. Renin-angiotensin system (ECF volume-dependent)
    a. Activated by blood loss, loss of Na^+, edema, upright posture
    b. Inhibited by atrial natriuretic factor (ANF)
2. K^+ concentration in plasma
3. ACTH
4. Autonomic nervous system

What are clinical manifestations of hyperaldosteronism?

1. Diastolic HTN without peripheral edema
2. Muscle weakness or paralysis (tetany)
3. Chronic headache
4. Polyuria/polydipsia (impaired renal concentrating ability)
5. Hypokalemic metabolic alkalosis

CASE 4

HPI: 48-year-old Caucasian male presents with paroxysmal hypertension despite the use of anti-hypertensive medications prescribed by his PCP. ROS is notable for episodic, sudden perspiration and chronic headaches. He was recently noted to have an adrenal mass on a CT scan performed to evaluate a kidney stone.

PMH: hypertension, hyperlipidemia, renal stones

PSH: none

Allergies: none **Medications:** Metoprolol, Amlodipine, Simvastatin

FH: (-) VHL, (-) NF1
SH: (+) tob, 1 PPD × 5 years; (-) ETOH; administrative assistant
ROS: As per above, (-) palpitations, (-) weight loss, (-) fatigue

PE:

Vitals	T 98.6	BP 150/110	P 100	RR 12
GA	calm			
HEENT	(+) hypertensive retinopathy			
Heart	RRR			
Lungs	no increased work of breathing on room air;;clear to auscultation bilaterally			
Abdomen	soft; non-tender; non-distended; no abdominal bruits			
Flank	benign			
Ext	(-) cyanosis; (-) clubbing; (-) edema			
Neuro	ambulates without assistance; no gross neurologic abnormalities			
CT abdomen/pelvis:	5.5 cm right adrenal mass (35 HU); (-) adenopathy; (-) extra-adrenal findings with normal-appearing kidneys bilaterally; no renal stones			

What is your differential diagnosis?

The differential diagnosis of uncontrolled HTN and an adrenal mass includes pheochromocytoma, Conn's syndrome, renal artery stenosis, and Cushing's syndrome, essential hypertension, benign adenoma, and adrenal cortical carcinoma.

What are appropriate screening lab tests?

BMP → WNL
Plasma metanephrines → elevated
Low dose dexamethasone suppression test → normal
AM plasma renin activity (PRA) → normal
AM plasma aldosterone activity (PAC) → normal

What is your assessment?

Adrenal mass with elevated plasma metanephrines suggests pheochromocytoma.

What is your next step?

24-hour total urinary metanephrines and fractionated catecholamines may be obtained to confirm diagnosis.

When is a MIBG scan indicated?

When metastatic pheochromocytoma, extra adrenal or recurrent pheochromocytoma is suspected.

What is MIBG?

Metaiodobenzylguanidine (MIBG) is a norepinephrine precursor.
MIBG is taken up in chromaffin cells of pheochromocytoma and provides a high sensitivity (83% to 100%) and superb specificity (95% to 100%) for identification of pheochromocytoma.

How would a pheochromocytoma appear on MRI imaging?

Pheochromocytomas typically exhibit high signal intensity on T2-weighted images; however, this finding is not diagnostic of a pheochromocytoma.

Is genetic testing indicated?

Nearly one quarter of patients who appear to have sporadic non-familial disease at diagnosis demonstrate germ-line mutations upon genetic testing.

Expert consensus recommends genetic testing for the RET, VHL, SDHB, and SDHD gene mutations for patients under 50 years of age, family history of pheochromocytoma, multiple lesions, bilateral disease, and malignant pheochromocytoma.

Of the known genetic mutations associated with pheochromocytoma, which has the greatest risk of malignant pheochromocytoma?

SDHD has been associated with a 30–50% rate of malignant disease when pheochromocytoma is noted.

How would you manage this patient?

Right adrenalectomy (open or laparoscopic).

How would you prepare this patient preoperatively?

1. α-blocker administration for catecholamine blockade
    a. Phenoxybenzamine 10 mg po TID (irreversible blocker) and titrated until normotensive
    b. Begin 1–3 weeks prior to surgery
    c. β-blocker can be initiated to help control arrhythmias and reflex tachycardia from α-blockade but should only be started after α-blocker
    d. Last dose provided the night prior to surgery to prevent post-operative hypotension
2. Volume expansion via aggressive intravenous fluid resuscitation and salt-loading
3. Alternatively, calcium-channel blockers can be used as an adjunct or in lieu of α-blockers

Note: The patient must be started on an α-blocker prior to β-blocker use. Selective β1 adrenoreceptor blockers, such as Atenolol and Metoprolol, are generally preferred.

BP goal: 120–130/80 mmHg in seated position; mid-postural hypotension (SBP > 90 mmHg) is acceptable

The patient tolerates his adrenalectomy without complication and undergoes an uncomplicated hospital course.

What is your follow-up?

1. Check pathology report: non-malignant pheochromocytoma
2. Repeat metabolic testing should be performed approximately 2 weeks after adrenalectomy to document normalization of chromaffin cell function
3. Annual biochemical follow-up beginning 6 months following surgery
4. Check BP, serum Cr, electrolytes at every clinic visit
5. Cross-sectional imaging annually

Long-term follow-up is paramount, since recurrences are reported in up to 15% of patients, even after 15 years following the initial resection of a localized lesion.

Note: Malignancy can currently only be defined by the presence of clinical metastases. Pathologic appearance and even local invasion are of only limited value in determining metastatic potential of a given lesion. A number of pathologic criteria to differentiate benign from malignant disease have been proposed, but to date there is no single histologic criterion agreed upon.

What are clinical signs and symptoms of pheochromocytoma?

1. Headache (60–90%)
2. Palpitations (50–70%)
3. Sweating (55–75%)
4. Sustained HTN (50–60%)
5. Pallor (40–45%)
6. Hyperglycemia (40%)
7. Paroxysmal HTN (30%)
8. Chronic weakness, tiredness (25–40%)
9. Psychologic symptoms (panic/anxiety) (20–40%)

Where does pheochromocytoma arise?

1. Adrenal medulla (75–90%)
2. Extra-adrenal (10–25%) = paragangliomas (they arise from chromaffin-producing neural crest tissue)
   a. Arise in the head, neck, thorax, abdomen, and pelvis (including bladder)
   b. Can arise between the aortic bifurcation and the root of the inferior mesenteric artery = organ of Zuckerkandl

What are hereditary forms of pheochromocytoma?

At least 5 genes—*RE*arranged *T*ransfection proto-oncogene *(RET)*, von Hippel-Lindau *(VHL)*, neurofibromatosis type 1 *(NF1)*, and mitochondrial succinate dehydrogenase subunits D and B genes *(SDHD, SDHB)*, are now associated with familial pheochromocytomas.

Syndromes associated with pheochromocytoma include von Hippel-Lindau, Neurofibromatosis type I, Multiple Endocrine Neoplasia types 2A and 2B, and Familial Paraganglioma Syndrome types 1 and 4.

What is classic "rule-of-ten" associated with pheochromocytoma and does it still apply to contemporary series?

1. 10% bilateral
2. 10% malignant
3. 10% extra-adrenal
4. 10% pediatric
5. 10% familial

Note: This rule has been repeatedly challenged and is likely not applicable to contemporary series. Up to 25% of pheochromocytomas may be extra-adrenal, familial cases account up to 30% of tumors at presentation, and only 5% are associated with malignant disease.

What are potential risks of untreated pheochromocytoma?

1. Congestive heart failure (Catecholamine-induced cardiomyopathy)
2. Malignant hypertension
3. Tachyarrhythmia
4. Cerebral vascular accidents
5. Hypertensive encephalopathy
6. Renal failure/renal infarction
7. Tumor hemorrhage

CHAPTER 2

BLADDER CARCINOMA

MARLA WARDENBURG, MD
PAUL CRISPEN, MD

CASE 1

HPI: 62-year-old Caucasian female is referred by her primary care physician after 2 episodes of painless gross hematuria. She was treated empirically for UTI, but urine cultures were negative each time. She is post-menopausal and is certain bleeding is not vaginal. She does have occasional stress incontinence and nocturia × 1, but denies dysuria, urgency, or obstructing voiding symptoms. AUASS 7/35. She does not have urethral discharge or dyspareunia. She has no history of recurrent UTI, urolithiasis, or flank pain. She does have a 25 pack year smoking history and quit 15 years ago.

PMH:

(+) hyperlipidemia
(+ hypothyroid
(-) UTI/pyelonephritis
(-) pelvic radiation
(-) stones
(-) analgesic abuse

PSH: lap cholecystectomy, open appendectomy as a child

Allergies: Sulfa **Medications:** Simvastatin, Levothyroxine

FH: (+) colon cancer
SH: (+) tob, 25 pack year; (-) ETOH
ROS: non-contributory

PE:

Vitals	T 99.1	BP 139/65	P 71	RR 14
GA	obese CF INAD			
HEENT	benign			
Breast	normal			
Heart	RRR			
Lungs	CTA			
Abdomen	soft; NT/ND; no masses, healed RLQ scar and lap incisions			
Flank	benign			
Pelvic	normal external genitalia, urethra and urethral meatus; no adnexal mass; no vaginal tenderness or masses, bladder mobile and non-distended			
Rectal	normal sphincter tone; no mass			
Ext	(-) CCE			
Neuro	non-focal			
Lymph nodes	(-) adenopathy			

What initial lab tests do you order?

UA → 15 RBC/HPF; (-) WBC
BMP → Cr 0.9 mg/dL, serum Ca normal
CBC → Normal
Cytology → (-) UC

What is your initial work up?

State that you would get upper tract imaging (CT urogram or IVP) and perform office cystoscopy.

1. Always check BMP prior to ordering contrasted imaging
2. Bilateral retrograde pyelograms + non-contrasted CT or MR urogram are alternatives to CT urogram/IVP in patients with poor renal function
3. Check pregnancy test for all women of childbearing age

Cystoscopy:	1 cm papillary tumor on left lateral wall, no active bleeding
CT Urogram:	collecting systems normal without filling defects

What do you do next?

State that you would obtain informed consent to take the patient to the OR for transurethral resection of bladder tumor (TURBT).

1. Obtain preoperative labs and administer prophylactic antibiotics
2. Discuss option for a single dose of post-TURBT intravesical therapy
3. Discuss need for paralysis with anesthesia provider and avoid bladder overdistention due to risk of obturator reflex for lateral wall resection
4. Complete eradication of visible tumor should be attempted

TURBT performed without complication, tumor resected entirely. A single dose of intravesical Mitomycin C was instilled for 1 hour in the post-op recovery area.

Pathology report: low-grade papillary Ta urothelial carcinoma; muscle was present in specimen and was not involved

How would you risk-stratify this patient?

She has low-risk non-muscle invasive bladder cancer.

AUA risk stratification for non-muscle invasive bladder cancer:

1. Low: low-grade Ta solitary lesion, primary, <3 cm or PUNLMP
2. Intermediate: recurrent within 1 year LG Ta, solitary LG Ta >3 cm, LG Ta multifocal, HG Ta $\leq$3 cm, LG T1
3. High: HG T1, any recurrent HG Ta, HG Ta >3 cm or multifocal, any CIS, any BCG failure in HG patient, any variant histology, any LVI, any HG prostatic urethral involvement

What is the role of perioperative intravesical chemotherapy?

For patients with pathologically confirmed non-muscle invasive bladder cancer (NMIBC), a single dose of intravesical Mitomycin C within 24 hours of TURBT is recommended to reduce risk of recurrence.

It is an option for patients with a papillary-appearing tumor but no pathologic diagnosis yet. The rationale for perioperative instillation includes the destruction of residual microscopic tumor at the site of TURBT and of circulating cells, thereby preventing reimplantation at the time of TURBT.

Mitomycin C is an alkylating agent that inhibits DNA replication. Due to the high molecular weight there is little absorption from the bladder into the systemic circulation.

The combination of TURBT and single dose Mitomycin C has been shown to decrease risk of recurrence by 17% compared to TURBT alone (for all risk groups of NMIBC). Common side effects include contact dermatitis and irritative voiding symptoms.

Perioperative Mitomycin C should not be administered to patients with a known or suspected bladder perforation following TURBT.

There is no evidence that multiple adjuvant instillations of either BCG or chemotherapy have additional benefit in patients at initial diagnosis of Ta low-grade bladder cancer.

What is your next step?

Surveillance cystoscopy in 3–4 months. No additional intravesical therapy is recommended for low-risk disease (small volume, low grade Ta, solitary tumor <3 cm).

Cystoscopy at 3 months is unremarkable. Cystoscopy 6 months after initial surveillance cystoscopy shows two 1cm papillary tumors at the left lateral wall and dome of bladder.

She undergoes repeat TURBT and a single dose of post-operative intravesical Mitomycin C. Pathology returns as low-grade Ta, again with non-involved muscle in specimen.

What is your recommendation?

She now has intermediate risk NMIBC. For patients with recurrent, multifocal, or large volume low-grade Ta, an induction course of BCG or Mitomycin C is recommended with the goal of preventing or delaying recurrence. Maintenance intravesical therapy is an option.

The patient undergoes an induction course of Mitomycin C (6 weeks) without complication. At 3 and 6-month cystoscopy she has no evidence of recurrence.

Discuss the TNM staging system for bladder cancer:

Bladder Cancer TNM Stage Classification:

Tx	Cancer stage unknown
To	No evidence of cancer
TIS	Carcinoma in situ
T1	Lamina propria
T2a	Muscularis propria—superficial muscle
T2b	Muscularis propria—deep muscle
T3a	Microscopic perivesical fat
T3b	Macroscopic perivesical fat
T4a	Involvement of adjacent structures (prostate, uterus, vagina)
T4b	Involvement of pelvic sidewall or abdominal wall
Nx	Nodal involvement unknown
N0	No evidence of nodal involvement
N1	Single lymph node 2 cm or less
N2	Single node (> 2 cm) or multiple nodes—all > 2 cm or ≤ 5 cm
N3	Single or multiple nodes > 5 cm
Mx	Distant metastasis unknown
M0	No evidence of distant metastasis
M1	Distant metastasis present

Republished with permission of Springer-Verlag New York Inc, from AJCC Cancer Staging Manual, Edge SB, 7th ed. ©2009; permission conveyed through Copyright Clearance Center, Inc.

What are potential risk factors for bladder cancer?

1. Tobacco abuse
2. Males > Females (3:1)
3. Age (90% of patients > 55-year-old at diagnosis)
4. Radiation
5. Chemical/occupational exposure—aromatic compounds (paint, dye, metal/petroleum)
6. Phenacetin—analgesic, no longer on market
7. Cyclophosphamide
8. Pioglitazone (Actos)
9. Schistosomiasis (SCC)
10. Chronic cystitis (SCC)—chronic UTI, indwelling Foley or CIC, bladder stones

What is the natural history of non-muscle invasive bladder cancer (CIS, Ta, T1)?

1. Ta—recurrence in 50–70%, progression in <5%
2. T1—recurrence in 70–80 %, progression in 50%
3. CIS—80% recurrence after TURBT, 20%–30% after BCG; 20% progress after a complete response to BCG

What factors influence time to recurrence of superficial UC (CIS, Ta, T1)?

1. Number of visible tumors
2. Tumor grade and stage
3. Tumor size > 3 cm
4. Concomitant CIS
5. Prior recurrence rate
6. Tumor present at initial 3-month cystoscopy

What are the risk factors for muscle invasion for superficial UC (CIS, Ta, T1)?

1. Tumor grade and stage
2. Carcinoma-in-situ
3. Tumor size (> 3 cm)

High stage or high-grade superficial lesions (high-grade T1, CIS) are aggressive with progression rates of 25% to 50% at 5 years (highest for multifocal high-grade T1 with CIS). Intravesical therapy is indicated at the time of presentation. If intravesical therapy fails, early cystectomy is warranted.

What are the main indications for intravesical chemotherapy or immunotherapy (BCG)?

Intravesical therapy is indicated for Ta, T1 or CIS urothelial carcinoma of the bladder.

3 main indications for intravesical therapy:

1. To reduce recurrence and progression in completely resected tumor

2. Eradication of CIS with or without associated papillary tumor
3. Eradication of residual papillary tumor after incomplete resection

Discuss intravesical chemotherapy agents used for superficial bladder cancer.

1. Thiotepa
    a. Alkylating agent/crosslinks DNA strands to prevent replication
    b. Side effect: myelosuppression. Check CBC before each instillation. Low molecular weight may permit systemic absorption
    c. Dose: 30–60 mg
2. Doxorubicin
    a. Antibiotic/inhibits DNA replication
    b. Side effect: skin irritation. Systemic absorption is rare
    c. Dose: 40–80 mg
3. Mitomycin C
    a. Alkylating agent/inhibits DNA replication
    b. Side effect: bladder irritation/contracture, contact dermatitis, hypersensitivity reaction. Systemic absorption rare due to high molecular weight
    c. Dose: 20–40 mg
    d. May be more effective at urine pH >6, consider giving 1.3 g sodium bicarbonate the night before instillation
4. Valrubicin
    a. Anthracycline/intercalating agent
    b. FDA approved for patients with CIS that is refractory to BCG and who are not candidates for radical cystectomy
    c. Side effect: irritative voiding symptoms, hematuria, UTI
    d. Dose: 800 mg

CASE 2

HPI: 60-year-old Caucasian male presents to the clinic complaining of bothersome urinary frequency and urgency for the past 2 years. He has had microhematuria on several UA's by his PCP over the past 2 years as well. He denies obstructive voiding symptoms. AUA symptom score 18/35 and potency is normal. He denies dysuria, gross hematuria, or incontinence. He has no significant urologic history, no history of STI, and no history of GU surgery or trauma. He does have a 20 pack year smoking history.

PMH: (-) stones
(-) prostatitis
hypertension
asthma (mild)

PSH: none

Allergies: none **Medications:** Albuterol inhaler, Lipitor, HCTZ

FH: (-) prostate cancer
SH: (+) tob, 20 pack year; (-) ETOH
ROS: non-contributory

PE:

Vitals	T 98.6	BP 140/60	P 90	RR 12
General	thin CM NAD			
HEENT	benign			
Heart	RRR			
Lungs	CTA			
Abdomen	soft; NT/ND			
Flank	benign			
GU	normal circumcised phallus; patent meatus; (B) testicles WNL			
Prostate	smooth and benign, 30 g; (-) nodules or induration			
Ext	(-) CCE			
Neuro	non-focal			
Lymph nodes	(-) adenopathy			

What initial lab tests do you order?

UA	→	12 RBC/HPF; (-) WBC
BMP	→	WNL; Cr 1.2 mg/dL
Cytology	→	(+) suspicious for urothelial carcinoma

Cytology is not part of the initial workup for asymptomatic microhematuria (3 or more RBC/HPF), but has a role for patients who are symptomatic (i.e., irritative voiding symptoms in the absence of infection) or who have risk factors for urothelial carcinoma.

What is your initial work up?

Get upper tract imaging (CT urogram or IVP) and perform office cystoscopy.

CT Urogram: entire collecting systems normal without filling defects
Cystoscopy: erythematous patch on the posterior wall; no obvious tumors

What do you do next?

State that you would obtain informed consent to take the patient to the OR for directed and random bladder biopsies. A TUR and a biopsy of the prostatic urethra may also be considered. Obtain preoperative labs and administer prophylactic antibiotics.

Biopsy and fulguration of red patch and random biopsies of the urinary bladder were performed. TUR biopsy of the prostatic urethra was performed as well.

Pathology report: Carcinoma in situ (CIS); muscle was present in specimen and was not involved;
Prostatic urethra normal; random bladder biopsies normal

What is your metastatic work-up?

You do not have to perform metastatic work-up for CIS.

What is your assessment?

60-year-old CM with CIS of urinary bladder.

1. CIS is a high-grade, flat lesion characterized by severe cellular dysplasia in the absence of discrete tumor formation
2. It may be found alone or adjacent to Ta or T1 disease
3. The presence of CIS is associated with a high risk of progression to muscle-invasive disease

What is your recommendation?

The first line treatment option for non-immunocompromised patients is an induction course of intravesical immunotherapy with BCG. BCG is superior to intravesical chemotherapy for CIS and other high-grade non-muscle invasive bladder tumors. Therapy with intravesical BCG decreases rates of tumor recurrence and progression.

BCG should be postponed for at least 2 weeks after TURBT.

Intravesical BCG (50mg/vial) is given once a week for 6 weeks (standard 6-week induction course).

The patient tolerates 6-week course of intravesical BCG without complications.

Discuss the theory of BCG.

BCG is an attenuated strain of Mycobacterium bovis. The immune response causes an intense local inflammatory reaction within the urinary bladder. It activates T-cells to attack abnormal urothelium and causes release of cytokines.

What are contraindications to BCG treatment?

BCG is contraindicated in patients with immunosuppression (HIV, lymphoma, leukemia, steroid use), as well as patients with a history of prior hypersensitivity reaction/sepsis after BCG. It is NOT contraindicated in patients with a positive PPD from receiving Bacillus Calmette-Guerin vaccine.

Under what conditions should intravesical BCG be postponed?

1. Recent resection (wait at least 2 weeks after TURBT)
2. Traumatic catheterization
3. Gross hematuria
4. Cystitis
5. Urinary tract infection or fever—check UA and temperature prior to administration

What is your follow-up?

Need to repeat urine cytology and cystoscopy every 3 months after the initial TURBT × 2 years, then every 6 months × 2 years, then annually thereafter. Upper tract imaging should be repeated every 1–3 years.

Maintenance BCG should be considered for responders. Maintenance therapy in BCG responders decreases rates of recurrence and can improve disease-free survival and complete response rates.

Standard maintenance schedule (SWOG regimen) is one intravesical BCG installation each week for 3 weeks at 3 and 6 months after the induction course, then every 6 months for 3 years in high risk patients and 1 year in intermediate risk patients.

You see the patient after 3 months.

Urine cytology: (+) UC
Cystoscopy: recurrent erythematous patch on the posterior wall; no obvious papillary or sessile tumors

Repeat biopsy of the red patch and the prostatic urethra was performed.

Pathology report: carcinoma in situ; prostatic urethra normal

What is your assessment?

60-year-old CM with recurrent CIS of urinary bladder after induction course of BCG.

What is your recommendation?

If CIS is not eradicated after an induction course of BCG, options include cystectomy or a second induction course of BCG.

The role of adding interferon α to BCG is not established. Interferon has antiproliferative effects and causes cytokine release, lymphocyte activation, and improved antigenic recognition of tumor cells. It is not FDA approved for intravesical therapy. Side effects include flu-like symptoms. Based upon the limited data available the benefit adding interferon α for this patient is unknown.

Decision is made to repeat induction course of BCG:

1. Intravesical BCG is given once a week for additional 6 weeks
   Tice BCG = 50 mg/vial
2. Repeat urine cytology and cystoscopy after second course of BCG

Urine cytology: (+) UC

Note: Prior BCG can cause suspicious urine cytology.

Cystoscopy: recurrent erythematous patch

What do you do now?

Re-biopsy the red patch and the prostatic urethra.

Biopsy of red patch was performed. Repeat biopsy of prostatic urethra was performed.

Pathology report: Carcinoma in situ of bladder and prostatic urethra

What is your assessment?

60-year-old CM with BCG—refractory recurrent CIS of bladder and prostatic urethra.

What does he need at this stage?

For patients with high-grade Ta, T1, or CIS that has recurred after 2 induction courses of intravesical therapy, cystectomy is recommended.

Additional options include intravesical therapy or consideration for a clinical trial. Valrubicin is FDA-approved for BCG-refractory CIS in patients who are not candidates for cystectomy.

The appropriate recommendation is:

1. Radical cystectomy with lymph node dissection
2. Urethrectomy if surgical margin negative at time of cystectomy
3. Urinary diversion—either a conduit or a continent reservoir

How would you prepare this patient?

State that you would obtain an informed consent by discussing the surgical procedure, indications, potential risks and complications.

State that you would obtain preoperative labs and tests to include a metastatic evaluation with CXR, CT scan of abdomen and pelvis, and bone scan if symptomatic or if the patient has elevated alkaline phosphatase.

In addition, a bowel prep may be considered but is not mandatory.

Prophylaxis for venous thrombosis should be performed with sequential compressive devices (SCDs) and subcutaneous heparin. To help facilitate bowel recovery following surgery, Alvimopan may be considered.

Standard use of an enhanced recovery program after surgery should be considered for cystectomy patients, which begins prior to the surgical procedure.

Labs:	BMP, CBC, PT/INR
Tests:	CXR, EKG, CT Abd/Pelvis
Blood:	T&C for 2 units PRBCs
Bowel prep:	optional

SCDs and subcutaneous heparin
IV antibiotics

Discuss your surgical technique.

Be prepared to discuss the operative procedure.

The Operation (Extended Pelvic Lymph Node Dissection)

Boundaries

1. Genitofemoral nerve—lateral
2. Bladder—medial
3. Common Iliac artery—proximal
4. Femoral canal—distal

An **extended** lymph node dissection includes the common iliac, external iliac, obturator, hypogastric, and presacral lymph nodes. An extended dissection may include nodes up to the level of the inferior mesenteric artery but is not necessary in cases of stage I disease.

A standard lymph node dissection includes the external iliac, obturator, and hypogastric lymph nodes.

The Operation (Radical Cystectomy)

1. Midline incision and mobilize the bladder and ureters
2. Divide the ureters at the insertion of the urinary bladder
3. Take down lateral pedicles of the bladder and the prostate
4. Ligate dorsal venous complex and divide the prostatic urethra
5. Deliver the specimen

The Operation (Ileal Conduit)

1. Harvest 12–15 cm length of terminal ileum at least 15–20 cm from the ileocecal valve
2. Maintain vascular supply
3. Close the mesenteric trap
4. Close the butt end of the loop
5. Swing the left ureter under the sigmoid mesentery to the right

6. Create Bricker (end to side—refluxing) or Wallace (end to end—refluxing) ureteral anastomoses to the ileal conduit
7. Place single J stents
8. Create rose-bud stoma
9. Place pelvic drain

The Operation (Continent Reservoir—e.g., Indiana Pouch, Florida Pouch)

1. Right colon and 10 cm distal ileum
2. Appendectomy
3. Narrow the catheterizable ileal segment with GIA stapler over 14–16 F catheter
4. Imbricate or reinforce ileocecal valve with silk Lembert sutures or cecal wrap
5. Colon folded into U-shaped segment and detubularized
6. Ureteral-colonic anastomosis
7. Place single J stents
8. Sew catheterizable channel to abdominal wall and ensure easy passage of catheter
9. Place pelvic drain

The Operation (Orthotopic Reservoir—e.g., Studer)

1. 50–55 cm ileum; 15–20 cm proximal to ileocecal junction
2. 10–15 cm proximal end for ureteral reimplantation
3. Place single J stents
4. Open antimesenteric side of the distal 40 cm
5. Fold into a sphere
6. Suprapubic tube is optional
7. Anastomose to prostatic urethra
8. Place pelvic drain

Discuss various metabolic abnormalities associated with bowel segments.

1.	Stomach	Hypochloremic hypokalemic metabolic alkalosis
2.	Jejunum	Hyponatremic hypochloremic hyperkalemic metabolic acidosis
3.	Ileum	Hyperchloremic hypokalemic metabolic acidosis
4.	Colon	Hyperchloremic hypokalemic metabolic acidosis
5.	Sigmoid	Hyperchloremic hypokalemic metabolic acidosis

Metabolic abnormalities	**Treatment**
Hyponatremic hypochloremic metabolic acidosis	oral sodium chloride; bicarbonate replacement; hydrate with fluids
Hyperchloremic hypokalemic metabolic acidosis	oral chloride restriction; bicarbonate replacement; oral/IV hydration; drain storage area with catheter

CASE 3

HPI: A 65-year-old Caucasian male presents to clinic with intermittent gross hematuria and with irritative voiding symptoms. He complains of nocturia × 2, urinary frequency every 1–2 hours during the day, and weak stream. He denies dysuria or incontinence. AUASS 11/35. He has a history of BPH, on tamsulosin with benefit.

PMH: BPH

PSH: L inguinal hernia repair

Allergies: none **Medications:** Tamsulosin

FH: (-) prostate cancer
SH: (-) tob; (-) ETOH
ROS: non-contributory

PE:

Vitals	T 97.9	BP 142/60	P 80	RR 16
GA	CM INAD, age appropriate			
HEENT	benign			
Heart	RRR			
Lungs	CTA			
Abdomen	mildly obese; soft; NT/ND			
Flank	benign			
GU	normal circumcised phallus; patent meatus; (B) testicles WNL			
Prostate	smooth and benign @ 35 g			
Ext	(-) CCE			
Neuro	non-focal			

What initial lab tests do you order?

UA → 5–6 RBC/HPF; (-) WBC; (-) bacteria
UCx → no growth
BMP → WNL; Cr 1.1 mg/dL

What would you do at this point?

Obtain CT urogram or IVP, urine cytology, and perform cystoscopy.

Cytology: (+) malignant cells - UC
CT-IVP: normal collecting system and ureters
Cystoscopy: 2cm sessile tumor (R) posterior wall; ureteral orifices uninvolved

What is your next step?

Obtain informed consent for TURBT in OR. Patient undergoes procedure without complication.

Pathology: high-grade T1, muscle present in specimen and uninvolved.

What is your next recommendation?

Advise patient to undergo repeat TURBT within 2–6 weeks. He agrees and pathology is again high-grade T1, with no invasion of muscularis propria.

What are the indications for repeat TURBT?

It is the standard to perform re-TURBT in patients with lamina propria invasion (T1) without the presence of muscularis propria in specimen. In the absence of muscularis propria, up to 20–40% of patients may have either residual tumor or unrecognized muscle-invasive disease.

Other situations in which repeat resection may be appropriate:

1. Incomplete initial TURBT
2. All T1 tumors
3. All high-grade tumors (except primary CIS)
4. Absence of muscle in specimen in initial resection (except primary CIS and low-grade Ta)

Even if muscle is present in the initial specimen, up to 30% of patients with T1 and high-grade Ta disease will be upstaged after repeat TUR.

What are his treatment options?

1. Immediate radical cystectomy—may be an option for patients with multiple or large (>3cm) high-grade T1 tumors, with high-grade T1 with concurrent CIS, high-grade T1 with lymphovascular invasion, or with micropapillary variant of UC. Radical cystectomy before induction intravesical therapy would be a very aggressive option for this patient
2. Intravesical chemotherapy
    a. Consider for immunocompromised patients. However, this is not the best treatment for high-grade tumors since response rates are not as good as for BCG, and the recurrence rates are high. It is an option if no residual disease is found after the second resection
    b. Intravesical chemotherapy (e.g., Thiotepa, Mitomycin C, etc.) does not have a good cure rate for high-grade T1, nor does it prevent progression of the disease.
3. Intravesical immunotherapy
    a. This is the best intravesical option for high-grade T1 disease. Intravesical BCG decreases recurrence rates and delays progression in patients with high-grade T1 of the bladder

2 weeks after TURBT, this patient was given Tice BCG once a week for 6 weeks.

After the fourth treatment, he developed low-grade temperature, urinary frequency, and dysuria.

What do you do now?

Treat him conservatively with Acetaminophen, Phenazopyridine, or anticholinergic. His irritative voiding symptoms resolve after 2 days.

After the sixth treatment, he develops a temperature of 103.3° and shaking chills.

What is your impression and treatment?

This patient has BCG sepsis, which can manifest rapidly and be associated with hypotension. He needs to be admitted to the hospital right away.

Early use of steroids may be lifesaving. He should be stabilized with IVF and anti-tuberculous medications ASAP—INH 300 mg/day, pyridoxine (vitamin B6 daily), rifampin 600 mg/day, and ethambutol 1200 mg/day. Cycloserine is no longer recommended. Recommend 6-month course of therapy.

In addition, obtain routine urine culture and blood cultures and begin broad-spectrum IV antibiotics. Fluoroquinolones have activity as 3rd line agents. He responds to quadruple anti-tuberculous medications and is discharged to home.

Is this patient a candidate for any future BCG therapy?

No! Any patient who has developed BCG sepsis should never receive intravesical BCG in the future.

At this point what do you recommend to your patient who cannot tolerate BCG and has recurrence?

1. For low-grade superficial tumors, Mitomycin C and other chemotherapeutic agents are options
2. For high-grade or invasive tumors, radical cystectomy should be considered

If he tolerated his induction BCG, what is your follow-up?

Maintenance therapy with BCG for minimum of 1 year for intermediate risk patients and 3 years for high risk patients. Start with full dose—may reduce to ½ strength for tolerance.

For high risk patients, 3 weekly maintenance BCG instillations at 3 months, 6 months, 12, 18, 24, 30, and 36 months (SWOG regimen).

How would you follow this patient?

1. Cystoscopy and cytology Q 3 months × 2 years, Q 6 months × 2 years, then annually
2. Upper tract study every 1–2 years for intermediate and high risk patients

At 3-month follow-up, cystoscopy reveals no evidence of disease.

Discuss the complications of BCG.

Minor complications:

1. Irritative voiding symptoms, hematuria
   a. NSAIDS, anticholinergic and Phenazopyridine
2. Low grade temperature and malaise
   a. Usually self-limited
   b. Acetaminophen
   c. Symptomatic treatment

Major complications:

1. Fever T <102° for > 48 hours
    a. Occurs in ~ 3% patients
    b. Stop BCG
    c. Urine culture for bacteria and AFB
    d. Broad-spectrum antibiotics and isoniazid (INH) daily
    e. Continue INH 300 mg QD for 3 months
    f. Pyridoxine 50 mg QD (to prevent neurotoxicity)
    g. Resume BCG when patient is asymptomatic
2. BCG Sepsis fever (T > 102) or signs of sepsis
    a. Stop BCG
    b. Hospitalization
    c. Obtain urine and blood cultures for bacteria and AFB
    d. IV steroids (Prednisolone 40 mg IV daily)
    e. INH 300 mg QD
    f. Rifampin 600 mg QD
    g. Pyridoxine 50 mg QD
    h. Ethambutol 1200 mg QD
    i. Fluoroquinolones preferred
    j. Add broad spectrum antibiotics to cover possible (-) Gm sepsis as well
    k. Duration of INH/Rifampin/Ethambutol—6 months
    l. Patients who survive BCG sepsis should not receive BCG in the future

    Cycloserine now recognized as ineffective.
    Check LFTs during INH therapy.

Note: This recommendation is different from anti-tuberculous therapy. CDC recommends a 6-month course of INH and Rifampin (plus Pyrazinamide for first 2 months of therapy) for both pulmonary and non-pulmonary TB.

What are the other side effects of BCG?

1. Granulomatous prostatitis ~ 45%
    a. 40% asymptomatic—no treatment
    b. 5% symptomatic—treat with INH/Rifampin × 3–6 months
2. Granulomatous orchitis/epididymitis < 2%
3. Cystitis ~ 50%—causes delay and dropout (due to intolerance) in 10%

What methods improve BCG tolerance?

1. Dose reduction
2. Space out treatments 2 weeks apart
3. Decrease dwell time

CASE 4

HPI: 45-year-old Caucasian male presents to the clinic complaining of painless gross hematuria for the past 3 months. He was treated with an antibiotic with no resolution. He denies significant irritative or obstructive voiding symptoms. He also denies dysuria, flank pain, or other UTI symptoms. He has no history of urethritis, STIs, or urethral discharge. He denies bone pain or unintentional weight loss. He has a history of BPH on Flomax with benefit. AUASS 9/35. Denies urinary incontinence. He does have a 15 pack year smoking history. Recent PSA is 2.5 ng/mL.

PMH:	(-) stones	(-) pelvic radiation
	(-) Cytoxan	(-) analgesic abuse
	(-) schistosomiasis	(+) BPH

PSH: none

Allergies: PCN

Medications: ASA QD, Tamsulosin 0.4mg/QD

FH: (+) lung cancer, colon cancer
SH: (+) tob, 15 pack year; (-) ETOH
ROS: non-contributory

PE:

Vitals	T 98.6	BP 140/60	P 90	RR 12
GA	thin CM in NAD			
HEENT	benign			
Heart	RRR			
Lungs	CTA			
Abdomen	soft; NT/ND; no palpable masses			
Flank	benign			
GU	normal circumcised phallus; adequate meatus; (B) testicles WNL			
Rectal	prostate smooth and benign @ 30 g; (-) nodules or induration normal sphincter tone			
Ext	(-) CCE			
Neuro	non-focal			
Lymph nodes	(-) adenopathy			

What initial lab tests do you order?

UA → grossly pink; too numerous to count RBC/HPF; (-) WBC
BMP → WNL; Cr 1.1 mg/dL
Cytology → (+) UC

What is your initial work up?

State that you would perform cystoscopy in the clinic.

Cystoscopy: multiple papillary and sessile tumors

What else do you need?

The patient needs to undergo an upper tract study. Since this patient has several sessile tumors which may be invasive, a CT scan of the abdomen and pelvis without and with contrast with delayed images prior to TURBT is the study of choice.

CT scan:	entire collecting systems normal; several filling defects within the bladder. No evidence of invasion no metastatic disease

What is your assessment?

45-year-old CM with multiple bladder tumors. Recommend TURBT with bimanual exam and random bladder biopsies with biopsy of the prostatic urethra.

Pre-op antibiotics—remember that he is allergic to PCN.

Stop his preventive ASA 7 days prior to his surgery (unless patient has significant cardiac risk factors).

He agrees to undergo the above procedure.

How do you proceed?

Obtain informed consent and preoperative labs. Give IV antibiotics.

TURBT of bladder tumors and random biopsies of the urinary bladder were performed. Prostatic urethra was biopsied via transurethral resection. Bimanual examination revealed a mobile urinary bladder with no 3-dimensional mass or bladder pedicle thickening.

Pathology report:	High grade multifocal UC with invasion of muscularis propria—superficial muscle; prostatic urethra normal; random bladder biopsies normal (no CIS).

What is your next step in clinical staging?

He needs metastatic work-up. State that you would obtain CXR, liver function tests (LFTs), alkaline phosphatase test. A bone scan is indicated if alkaline phosphatase is elevated or the patient is symptomatic. He should also get a Hemoccult test.

Chest x-ray	WNL
Liver function tests	WNL
Alkaline phosphatase	WNL
Hemoccult	(+) heme

What is his clinical stage?

Clinical stage T2aN0M0 UC of the bladder.

What are his treatment options?

State the treatment options which include the following:

1. TURBT (±intravesical immunotherapy)—this option is limited to highly selective patients with extensive comorbid disease or poor performance status, and is not appropriate for this patient

2. Partial cystectomy—a consideration in selected patients with solitary tumors that are not good radical cystectomy candidates; not a good choice for this patient
3. Bladder-sparing approach consisting of TUR + chemotherapy + radiation—requires highly interdisciplinary approach and close follow-up, and is not appropriate in a relatively young and overall healthy patient with multifocal disease
4. Radical cystoprostatectomy (± neoadjuvant chemo) with PLND and urinary diversion—this is the "gold standard" for treating non-metastatic muscle-invasive bladder cancer

What is the role of neoadjuvant chemotherapy?

For clinical stage T2-T4a N0M0 UC of the bladder, neoadjuvant chemotherapy has been shown to provide an overall survival benefit and is recommended by the EAU and NCCN for patients who can tolerate it (and in whom renal function permits).

Neoadjuvant therapy consists of 3–4 cycles of multi-agent Cisplatin-based chemotherapy.

Standard regimens:

1. MVAC (Methotrexate, Vinblastine, Doxorubicin, Cisplatin)
   a. Higher rate of neutropenia, sepsis, mucositis, alopecia, fatigue
   b. Methotrexate: mucositis; myelosuppression
   c. Vinblastine: neurotoxicity
   d. Adriamycin: cardiotoxicity
   e. Cisplatin: nephrotoxicity
2. GC (Gemcitabine, Cisplatin)
   a. Gemcitabine: thrombocytopenia and anemia
   b. Cisplatin: nephrotoxicity

Patient wishes to proceed with neoadjuvant chemotherapy and cystoprostatectomy with continent urinary diversion.

He has family history of colon cancer and has positive Hemoccult test. He needs barium enema or flexible colonoscopy prior to surgery.

Colonoscopy was performed and findings were normal.

He undergoes 4 cycles of GC and tolerates it well. Surgery is planned for 1–2 months after completion of chemotherapy.

What is your pre-op work-up?

First, obtain a re-staging CT chest, abdomen, pelvis to evaluate response to neoadjuvant therapy and for disease progression or metastasis. CT is performed and shows no evidence of progression.

State that you would obtain an informed consent, order preoperative labs, give preoperative antibiotics and DVT prophylaxis, and have enterostomal therapist to mark the stoma.

In addition, a bowel prep may be considered but is not mandatory. Stop ASA 7 days before surgery. To help facilitate bowel recovery following surgery, Alvimopan may be considered.

Standard use of an enhanced recovery program after surgery should be considered for cystectomy patients which begins prior to the surgical procedure.

The Operation:

Be prepared to discuss your surgical approach. You are going to perform an extended pelvic lymph node dissection, a cystoprostatectomy, and urinary diversion (e.g., Indiana pouch, neobladder, or ileal conduit).

Describe the Surgical Technique.

The Operation (Pelvic Lymph Node Dissection)

Boundaries for the pelvic lymph node dissection include the following:

1. Genitofemoral nerve—lateral
2. Bladder—medial
3. Aortic bifurcation—proximal
4. Femoral canal—distal

Note: An extended LND that includes the common iliac and the pre-sacral lymph nodes may provide more accurate staging, increase the total lymph node count, and improve survival.

The Operation (Cystoprostatectomy—for males)

1. Midline incision
2. Divide urachus and vasa
3. Take down lateral pedicles of the bladder and prostate
4. Incise the peritoneum in the rectovesical cul-de-sac
5. Incise endopelvic fascia
6. Preserve the neurovascular bundles
7. Ligate dorsal venous plexus
8. Transect the urethra

The Operation (Continent Reservoir—e.g., Indiana Pouch)

1. Right colon and 10 cm distal ileum
2. Appendectomy
3. Narrow the catheterizable ileal segment with GIA stapler
4. Imbricate ileocecal valve with silk Lembert sutures
5. Ureteral anastomosis into colon pouch
6. Place ureteral stents
7. Sew catheterizable channel to abdominal wall
8. Place pelvic drain

During the operation, you find that it is impossible to perform a continent cutaneous pouch or an orthotopic neobladder. You have not yet divided the bowel. You decide to perform an ileal conduit.

How do you proceed?

The Operation (Ileal Conduit)

1. Harvest 12–15 cm length of terminal ileum at least 15–20 cm from the ileocecal valve
2. Maintain a vascular supply

3. Perform enteroenterostomy
4. Close mesenteric trap above the conduit
5. Pass the left ureter behind the sigmoid mesentery
6. Close the butt end of the loop
7. Ureteroileal anastomosis
8. Tack the butt end of the loop in the retroperitoneum
9. Place single J ureteral stents
10. Mature the stoma
11. Place pelvic drain

What if pelvic nodes are positive on preoperative imaging?

1. Biopsy is indicated if the nodes are outside the pelvis
2. If nodes are positive, chemotherapy is indicated

What if unsuspected grossly enlarged nodes are found at cystectomy?

1. Is all the disease resectable?
    a. If yes, proceed with cystectomy and extended PLND
    b. Recommend adjuvant chemotherapy
2. Abort case and treat with chemotherapy when:
    a. Bulky adenopathy is unresectable
    b. Desmoplastic periureteral mets
    c. Rectal wall is invaded
    d. Bladder fixed and unresectable

He tolerated his operation well and was transferred to the recovery room.

What are the indications for partial cystectomy?

1. Single, primary tumor with no CIS (perform mapping biopsies)
2. Location suitable for bladder preservation away from ureteral orifices (i.e., dome)
3. High grade, focal, muscle invasive tumor with complete or partial response to systemic chemotherapy
4. Tumor that is amenable to complete excision with negative margins
5. Tumor in bladder diverticulum (solely)
6. Patients with urachal adenocarcinoma—resect posterior rectus sheath, urachus, and bladder dome (en-bloc)
7. Patients who will have sufficient bladder capacity after partial cystectomy (perform cystogram first)

What are complications of partial cystectomy?

1. Tumor recurrence
2. Vesicocutaneous fistula
3. Ureteral obstruction
4. Urine leak
5. Reduced bladder capacity
6. Urge incontinence

Note: Bilateral pelvic lymph node dissection must be performed in patients undergoing partial cystectomy. Bladder relapse rates remain high despite strict inclusion criteria.

What is the role of bladder-preserving treatment for muscle-invasive bladder cancer?

Bladder-sparing approach may be considered for patients who are medically unfit for major surgery or who refuse cystectomy. This consists of repeat TURBT (with removal of all visible tumor that can be safely resected) followed by concurrent chemotherapy and radiation.

XRT is administered with a radiosensitizing systemic chemotherapeutic agent such as Cisplatin or 5-fluorouracil. Generally, 45–55 Gy to the whole bladder and lymph nodes with 20 Gy to the tumor is given. 22–47% of patients will require cystectomy due to incomplete response.

If bladder cancer is still present on post-treatment imaging and is still resectable, radical cystectomy is recommended. If the tumor is unresectable or metastatic, systemic chemotherapy may be offered.

What are poor prognostic features for treating patients with MIBC with bladder-sparing therapy?

1. Hydronephrosis
2. cT3b, cT4 disease
3. Low Hgb
4. CIS—does not respond to XRT
5. Residual disease after TURBT

What are indications for external beam radiation therapy?

1. As a sole treatment modality
    a. Rarely used as monotherapy
    b. Monotherapy best for patients with significant pulmonary or cardiac comorbidities for whom risks of surgery are prohibitive and for whom systemic chemotherapy is not an option
    c. Associated with low cure rates (20%–30%)
2. Combined radiation and chemotherapy
    a. Survival is stage dependent
    b. Debulking TURBT improves response
    c. Radiosensitizing chemotherapy (Cisplatin, 5-FU, or Taxol) increases response rate 10%–15%
3. Post-op adjuvant XRT for patients who have no evidence of disease is discouraged
    a. Local objective response rate of 55–75%
4. Post-operative radiation therapy
    a. Survival rate for patients with muscle invasive disease is dismal
    b. Routine use of post-operative radiation therapy discouraged

CASE 5

HPI: 55-year-old Caucasian male status post radical cystectomy for muscle invasive urothelial carcinoma of the bladder with Studer orthotopic neobladder. Post-operative course is initially uncomplicated, then urine output decreases on POD #5. Surgery was routine and there were no complications. Diverting ureteral stents, Foley catheter, SPT, and JP drain were placed. Clear serous fluid is coming from all drains. He has new fever as well as nausea and vomiting.

PMH: HTN, bladder cancer

PSH: Cystectomy, Studer neobladder

Allergies: none **Medications:** none

FH: non-contributory
SH: (-) tob; (+) ETOH
ROS: non-contributory

PE:

Vitals	T 101.2 BP 160/60 P 100 RR 16
GA	middle-aged CM in mild distress
HEENT	benign
Heart	RRR
Lungs	CTA
Abdomen	moderately distended; hypoactive bowel sounds; incision intact
Flank	(-) CVAT
GU	normal phallus; adequate meatus (B) testicles WNL
Rectal	normal
Ext	(-) CCE
Neuro	non-focal
JP drain	clear serous fluid; 1500 mL/ 24h
SPT	clear serous fluid; 200 mL/24h
Foley	clear serous fluid; 250 mL/24h
(B) stents	draining clear urine

What is your initial step in evaluation?

Irrigate both stents, Foley and SPT.

All catheters and stents irrigate easily, with minimal mucus from Foley and SPT.

What initial lab tests do you order?

UA	2–3 RBC/HPF; (-) WBC
UCx	no growth
CBC	WBC 14 K/μL; Hgb 11 g/dL; Hct 33%; platelets 275 K/mm^3
BMP	Na 137 meq/L; K 3.9 meq/L;

	Cl 108 meq/L; CO2 21 meq/L; BUN 46 mg/dL; Cr 2.7 mg/dL
JP fluid	Cr 18.0 mg/dL

What is your assessment?

55-year-old CM with decreased urine leak from orthotopic neobladder and possible urinary tract infection.

What is your differential diagnosis?

Differential diagnosis includes urine leak at these sites: pouch suture line, ureteroenteric anastomosis, or urethral anastomosis.

What do you do at this point?

This patient needs pouchogram via SPT as well as stentogram.

Pouchogram: intact suture line of the pouch; (-) extravasation
Stentogram: (+) extravasation at ureteroenteric anastomosis

What is your next step in management?

Try conservative measures and wait for the output to decrease. Do not be in a rush to explore the patient. Things to consider in sequence are:

1. Make sure the SPT and Foley irrigate easily, are free of mucus, and freely draining
2. Take suction off the JP drain
3. Cautiously manipulate the JP away from the anastomotic site
4. Place percutaneous nephrostomy tubes to maximally divert the urine

You followed this algorithm and his leak stopped eventually.

Note: If there is a continued leakage of significant amounts of urine despite waiting an adequate amount of time or if there is a large pouch leak, re-operate and repair the leakage site.

What are intraoperative complications of radical cystectomy?

1. Hemorrhage
2. Tumor spillage
3. Rectal injury
4. Vascular injury
5. Nerve injury (i.e., obturator nerve)

What are post-operative complications of radical cystectomy?

1. Prolonged ileus
2. Wound infection
3. Urinary leak
4. Small bowel obstruction
5. DVT/PE
6. Intestinal leak
7. Wound dehiscence
8. Fistula formation

9. Hemorrhage
10. Urinary/renal obstruction
11. Pyelonephritis

Name the different types of urinary diversions and indications for use.

1. Conduit
    a. Ileal conduit
        i. 12–15 cm length
        ii. Gold standard of urinary diversion
    b. Jejunal conduit
        i. Use only as last resort
    c. Transverse or sigmoid conduit
        i. Transverse colon useful after pelvic irradiation
        ii. Sigmoid conduit useful in total pelvic exenteration

    Note: Sigmoid conduit should be avoided in:

    Irradiated pelvis: superior hemorrhoidal artery is often sacrificed during the harvest; distal colon and rectum have insufficient blood supply due to radiation changes
    Cystectomy cases: if internal pudendal artery is damaged during cystectomy, blood supply to the rectum is compromised

2. Continent reservoir
    a. Indiana pouch
        i. Entire right hemicolon
        ii. Distal 10 cm ileum
        iii. Perform appendectomy
        iv. Imbricate ileocecal valve
3. Orthotopic neobladder
    a. "Hemi-Kock"
        i. Use 70 cm ileum
        ii. M or W configuration
        iii. LeDuc ureteral implants
        iv. Preserve distal 15 cm ileum
    b. Mainz pouch
        i. Ileocecal segment (15 cm cecum; 30 cm ileum)
        ii. W configuration
        iii. Tunneled ureteral anastomosis
        iv. Perform appendectomy
    c. Ileal neobladder (i.e. Studer)
        i. Use 50–55 cm ileum
        ii. Proximal 10–15 cm of ileum tubularized for ureteral anastomosis
        iii. Leave distal 20 cm of ileum intact; preserve the ileocecal valve

CASE 6

HPI: 68-year-old African-American male status post radical cystectomy for muscle invasive (stage T2bN0M0) urothelial carcinoma of the bladder with ileal conduit. Post-operative course initially uncomplicated until increased drain output on POD #6. Radical cystoprostatectomy with ileal conduit (without urethrectomy) was performed without complication. A Bricker style ureterointestinal anastomosis was performed and his ureteral stents were accidentally removed during his appliance change on POD #3. A JP drain was placed and it is now draining clear serous fluid. The patient has fever and abdominal distention.

PMH: muscle invasive bladder cancer (UC)

PSH: cystoprostatectomy
ileal conduit

Allergies: none **Medications:** none

FH: non-contributory
SH: (+) tob; (-) ETOH
ROS: non-contributory

PE:

Vitals	T 101.3	BP 140/70	P 90	RR 14
GA	elderly AAM in mild distress			
HEENT	benign			
Heart	RRR			
Lungs	CTA			
Abdomen	moderately distended; hypoactive bowel sounds; incision intact stoma pink and well-perfused			
Flank	(-) CVAT			
GU	normal phallus; adequate meatus (B) testicles WNL			
Rectal	normal			
Ext	(-) CCE			
Neuro	non-focal			
JP drain	clear serous fluid; 1600 mL/24h			
Stoma bag	clear serous fluid; 300 mL/24h			

What initial lab tests do you order?

UA	→	2–3 RBC/HPF; (-) WBC
UCx	→	no growth
CBC	→	WBC 12 K/μL; Hgb 10 g/dL; Hct 30%; platelets 332 K/mm^3
BMP	→	Na 132 meq/L; K 3.6 meq/L; Cl 110 meq/L; CO2 21 meq/L; BUN 42 mg/dL; Cr 3.0 mg/dL
JP fluid	→	Cr 31.0 mg/L

What is your assessment?

68-year-old AAM with increased drain output after ileal conduit and urine leak. Differential diagnosis includes urine leak at the butt end of the conduit or ureteroileal anastomosis.

What do you do at this point?

This patient needs loopogram. You cannot perform a stentogram since stents were accidently removed on POD #3.

Loopogram: intact suture line at the butt end; (+) extravasation at area of suspect ureteral intestinal anastomosis.

Non contrast CT scan: Fluid collection at butt end of ileal conduit. Moderate left hydronephrosis and hydroureter down to the level of the ileal conduit.

What is your next step in management?

Try conservative measures and wait for the output to decrease. Do not be in a rush to explore the patient!

Things to consider in sequence are:

1. Place a Foley catheter in the loop
2. Take suction off the JP drain
3. Cautiously manipulate the JP away from the anastomotic site
4. Place (L) percutaneous nephrostomy tube to maximally divert the urine
5. Percutaneously drain undrained fluid collections

The urine leak persists, and the patient becomes sicker with febrile episodes.

What do you do next?

The patient is taken to the operating room and the leak is repaired. An internal stent is placed at the time of surgery.

The patient has an uncomplicated post-operative course. The stent was removed after a normal stentogram. The JP drain was removed when the output became minimal. Serum creatinine returned to normal, 1.4 mg/L.

What is your follow-up?

1. Serum Cr at every clinic visit
2. Urine cytology Q 3–6 months for 2 years and then as clinically indicated
3. Urethral wash for cytology Q 6–12 months, particularly if CIS was present in the bladder or in the prostatic urethra
4. CXR and CT imaging of the abdomen and pelvis (including upper tract urothelium) every 3 to 6 months for 2 years and then as clinically indicated

2 years later, his urethral washings became positive for malignancy.

What do you do now?

Obtain recent upper tract imaging, CT scan of abdomen and pelvis and perform physical exam including careful evaluation for inguinal lymphadenopathy.

CT-IVP:	2 cm mass and filling defect at (L) distal uretero-ileal anastomosis and hydroureteronephrosis
LFTs:	normal

What is your next step?

Percutaneous nephrostomy, antegrade study of the (L) kidney, and stent placement. Send off urine cytology at the time of percutaneous tube placement.

Antegrade study:	contrast barely passes (L) ureteroileal anastomosis; there is a filling defect; an antegrade stent was placed successfully
Urine cytology:	positive for UC

Note: Antegrade stent was placed to open up the obstruction and also for ease of identifying the ureter at the time of uretero-ileal revision.

What is the treatment of choice?

1. Reoperation with excision of the (L) distal ureter and ureteroenteric anastomosis. Be careful to obtain negative ureteral margins intraoperatively. Consider on the table ureteroscopy and perform nephroureterectomy if multifocal disease is identified
2. Urethrectomy

What are risk factors for urethral recurrence following radical cystectomy?

1. History of multifocal non-muscle invasive urothelial carcinoma
2. History of bladder CIS
3. Bladder cancer stage
4. History of urothelial carcinoma of the prostate
5. Non-orthotopic urinary diversion

What are indications for urethrectomy?

Men

1. Diffuse CIS of the prostatic urethra or ducts
2. Tumor invasion into the prostatic stroma
3. CIS or frank tumor at the apical margin

Women

1. CIS or tumor involvement at the bladder neck or urethra
2. Presence of multifocal CIS
3. Tumor involving the anterior vaginal wall

CASE 7

HPI: 65-year-old African-American male with a history of prostate cancer presents after 1 episode of painless gross hematuria. He has no history of UTI, nephrolithiasis, or sickle cell disease. Low risk T1c prostate cancer was treated with external beam radiation therapy 5 years ago. He denies irritative or obstructive voiding symptoms; AUASS 5/35. Reports normal potency, libido, and ejaculation. Last PSA was 0.9 ng/mL, nadir following radiation therapy for prostate cancer was 0.6 ng/mL.

PMH: prostate cancer

PSH: right inguinal hernia repair

Allergies: none **Medications:** none

FH: none
SH: (+) tob, 30 pack year; (-) ETOH
ROS: non-contributory

PE:

Vitals	T 98.6	BP 140/60	P 90	RR 12
GA	thin AAM INAD			
HEENT	benign			
Heart	RRR			
Lungs	CTA			
Abdomen	soft; NT/ND; (-) masses			
Flank	(-) CVAT			
GU	normal circumcised phallus; adequate meatus; (B) testicles WNL			
Rectal	normal tone; flat and smooth firm prostate; (-) nodules or induration			
Ext	(-) CCE			
Neuro	non-focal			

What initial lab tests do you order?

UA → TNTC RBC/HPF; (-) WBC
BMP → WNL
CBC → Hgb 13 g/dL
Cytology → (+) UC

What is your initial work-up?

State that you would obtain upper tract studies (IVP or CT urogram) and perform office cystoscopy.

Cystoscopy: multiple papillary and sessile tumors
CT urogram: entire collecting systems normal; several filling defects within the bladder

What is your assessment?

65-year-old AAM with multiple bladder tumors and biochemical recurrence following radiation therapy for prostate cancer. He needs bimanual examination under anesthesia and TURBT.

How do you proceed?

Obtain informed consent and preoperative labs. Give IV antibiotics.

TURBT of bladder tumors and random biopsies of the urinary bladder were performed. Prostatic urethra was biopsied as well. Bimanual examination revealed a non-fixed urinary bladder with no 3-dimensional mass or bladder pedicle thickening.

Pathology report:	high grade UC with invasion of lamina propria (T1); no muscularis propria is seen; prostatic urethra normal; random bladder biopsies normal

What do you do now?

Need to repeat TURBT to obtain muscle to improve clinical staging accuracy.

Repeat TURBT was performed and pathology report revealed invasion into the deep muscle (T2).

What is your metastatic work-up?

State that you would obtain liver function tests (LFTs), alkaline phosphatase and CXR. CT urogram was recently performed.

Liver function tests	WNL
Alkaline phosphatase	WNL
Chest x-ray	WNL

What is his clinical stage?

65-year-old AAM with clinical stage T2N0M0 UC of the bladder.

What are your treatment options?

State that the treatment options include the following:

1. Cystoprostatectomy with or without neoadjuvant chemotherapy with urinary diversion
    a. Gold standard for muscle invasive disease
    b. Consider transverse colon conduit if ileum damaged due to pelvic radiation
2. TURBT with combination radiation and radiosensitizing chemo (trimodality therapy)
    a. He already received external beam radiation for his prostate cancer. Additional radiation is contraindicated
3. TURBT with intravesical chemotherapy or immunotherapy
    a. A possibility for highly selective patients with no invasive tumor on re-resection, or who are medically unfit for both cystectomy and systemic chemotherapy

He is interested in cystoprostatectomy with urinary diversion.

How do you proceed?

State that you would obtain an informed consent, pre-operative antibiotics, DVT prophylaxis, and have enterostomal therapist to mark the stoma.

To help facilitate bowel recovery following surgery, Alvimopan may be considered.

Standard use of an enhanced recovery program after surgery should be considered for cystectomy patients which begins prior to the surgical procedure.

Be prepared to discuss your surgical approach. You are going to perform a cystoprostatectomy, extended PLND and a urinary diversion.

He had pelvic irradiation for his prostate cancer. Consider transverse colon for urinary diversion if distal ileum does not appear normal.

How do you perform pelvic lymph node dissection?

Boundaries for the pelvic lymph node dissection include the following:

Aortic bifurcation	proximal
Femoral canal	distal
Genitofemoral nerve	lateral
Bladder	medial

During PLND, you encounter an enlarged external iliac lymph node.

What do you do now?

Complete the PLND and proceed with cystoprostatectomy.
Presence of lymphadenopathy does not preclude stopping a potentially curative operation.
Long-term survival with minimal lymph node burden is possible and surgery should proceed.

Describe your surgical technique.

The Operation (Radical Cystectomy)

1. Midline incision
2. Divide urachus and vasa
3. Divide ureters at level of the bladder
4. Take down lateral pedicles of the bladder and prostate
5. Ligate dorsal venous complex
6. Transect the urethra
7. Deliver the specimen

During the operation, a rectal tear is made as the prostate is being dissected off the anterior rectal wall.

What is your management of this complication?

Complete the cystectomy. Perform diverting colostomy. Close the tear primarily in multiple layers and cover the area of injury with omental flap.

After completing the cystectomy, transverse loop conduit is created using Bricker style anastomosis and urinary diversion stents are placed; 2 JP drains are placed.

On post-operative day 7, there is increased output from the JP drains.

What do you do now?

Send off the fluid from the JP for creatinine and compare to serum creatinine.

The fluid creatinine level is 80.0 mg/dL, and serum creatinine is 1.5 mg/dL.

What is your assessment, and what do you do next?

This patient has a urine leak from his urinary system. Need to get KUB to assess location of the JP drains.

KUB: drains are next to ureterocolonic anastomosis; stents are in good position

You gently advance the drains away from the anastomotic site but urine leak persists.

Now what is your plan?

Insert a stomal catheter to decompress the colon conduit and perform a loopogram.

Loopogram: bilateral hydronephrosis and significant extravasation at right ureterocolonic anastomosis

He now develops fever and abdominal pain.

What is your next step?

Obtain abdominal CT scan to rule out urinoma.

CT scan: large collection of urine at anastomosis and (B) hydronephrosis

How do you manage this?

Place bilateral percutaneous nephrostomy tubes and also place percutaneous drain to decompress the urinoma.

He does not respond to drainage tubes and urine leakage persists.

What do you need to do at this point?

He needs to be explored for revision of his ureterocolonic anastomosis.

You take him to surgery and revise his ureterocolonic anastomosis. He recovers well from his operation.

What are some metabolic complications of post-cystectomy urinary diversion?

1. Electrolyte abnormalities
2. Altered sensorium → increased ammonia levels
3. Altered hepatic metabolism
4. Pyelonephritis → more common with Proteus or Pseudomonas
5. Metabolic acidosis → osteomalacia
6. Renal and reservoir calculi → struvite stones; most commonly associated with hyperchloremic metabolic acidosis
7. Adenocarcinoma → ureterosigmoidostomy ureteral anastomosis site at risk
8. Short bowel syndrome → vitamin B_{12}, bile salt, calcium, and folic acid malabsorption

Note: The ileum is major site of vitamin B_{12} absorption. Malabsorption of vitamin B_{12} results in anemia and neurologic abnormalities. The ileum is the major site of bile salt reabsorption. Lack of ileum to a significant degree allows bile entry into colon, which causes mucosal irritation and diarrhea. Loss of significant amount of jejunum may result in malabsorption of fat, calcium, and folic acid.

What are treatment options for regionally advanced bladder cancer?

1. Primary chemotherapy
   a. Methotrexate, Vinblastine, Adriamycin, Cisplatin (MVAC)
      i. Partial response: 70%
      ii. Complete response: 40%
   b. Gemcitabine and Cisplatin
      i. Similar response rates to MVAC (although studies are limited)
      ii. Associated with less toxicity
      iii. Requires adequate renal function
      iv. Carboplatin often substituted for Cisplatin in elderly patients and in those with renal insufficiency
2. Neoadjuvant chemotherapy (3 to 4 cycles) and cystectomy
   a. Multi-agent Cisplatin based combinations (single agent not effective)
   b. Recommended for patients with T3, T4, N+, or LVI
   c. Neoadjuvant chemo for T2 patients less clear unless LVI present
   d. Causes downstaging of locally advanced disease
      i. Clinical downstaging: 60%
      ii. Pathological downstaging: 30%
   e. Provides better survival probability than surgery alone
   f. Most patients proceed to cystectomy following neoadjuvant chemo
3. Adjuvant chemotherapy after cystectomy
   a. Allows early removal of primary tumor
   b. Best for pathologic stage T3a
   c. Patients are treated based on pathologic staging
   d. 20–50% patients do not complete the course of treatment
   e. Survival advantage not consistently demonstrated in clinical trials. Neoadjuvant chemotherapy remains standard of care

CASE 8

HPI: 54-year-old African-American female is referred by her primary care physician for microscopic hematuria. She initially presented to her PCP due to persistent urinary urgency, frequency, and dysuria, with negative urine cultures and no improvement with antibiotics or anticholinergics. She has no history of UTIs, urolithiasis, or flank pain. AUASS 15/35. She denies urethral discharge or dyspareunia. She has a 30 pack year smoking history and quit 7 years ago. She denies fevers, bone pain, or unintentional weight loss.

PMH:
(-) stones
(-) Cytoxan
(-) schistosomiasis
(-) pelvic radiation
(-) analgesic abuse

PSH: TAH/BSO—symptomatic uterine leiomyoma

Allergies: none **Medications:** Oxybutynin for urinary frequency

FH: (+) breast cancer
SH: (+) tob, 30 pack year; (-) ETOH
ROS: non-contributory

PE:

Vitals	T 98.6	BP 120/60	P 60	RR 12
GA	thin AAF INAD			
HEENT	benign			
Breast	normal			
Heart	RRR			
Lungs	CTA			
Abdomen	soft; NT/ND; no masses, healed lower abdominal incision			
Flank	benign			
Pelvic	normal external genitalia, urethra and urethral meatus; no adnexal mass; left bladder pedicles indurated but vaginal wall otherwise normal, no 3-dimensional mass or fixation			
Rectal	normal sphincter tone; no mass			
Ext	(-) CCE			
Neuro	non-focal			
Lymph nodes	(-) adenopathy			

What initial lab tests do you order?

UA	→	TNTC RBC/HPF; (-) WBC
BMP	→	Cr 1.3 mg/dL, serum Ca normal
CBC	→	normal
Cytology	→	(+) urothelial carcinoma

What is your initial work up?

State that you would obtain an upper tract study (reasonable to do first based on the pelvic exam and the positive cytology).

CT urogram:	Moderate left hydroureteronephrosis, thickened left bladder wall with possible bladder filling defect; right collecting system clear; left ureter and renal pelvis not completely evaluated; no pelvic or retroperitoneal lymph node mets; no obvious distant mets

What is your assessment?

54-year-old AAF with probable invasive bladder cancer and partial left renal obstruction. She needs bimanual examination under anesthesia, TURBT, bladder biopsies, and attempted left retrograde pyelogram followed by placement of left ureteral stent.

How do you proceed?

Obtain informed consent and preoperative evaluation. Give IV antibiotics.

Cystoscopy reveals a 3 cm tumor involving the left lateral wall extending to involve the left ureteral orifice. Other satellite tumors are located on the bladder dome and on the posterior bladder wall. Good bladder capacity.

TURBT along with random biopsies of the bladder neck are performed. The left ureteral orifice could not be identified and a stent is not placed. EUA was not different from the initial pelvic exam—indurated left bladder pedicles but no 3-dimensional mass.

Pathology report:	left lateral wall—high grade UC with invasion of muscularis propria, high grade non-invasive UC bladder dome and posterior wall, bladder neck biopsies normal; no CIS; lymphovascular invasion (LVI) is present

What is your next step in clinical staging?

She needs metastatic evaluation. State that you would obtain CXR or chest CT, liver function tests (LFTs).

Note: Patient has family history of breast cancer and has no recent mammography.

Chest x-ray	WNL
Liver function tests	WNL
Mammogram	WNL

What is her clinical stage?

Clinical stage T2b versus T3a N0M0 UC, left ureteral obstruction, and LVI.

What are her treatment options?

State the treatment options which include the following:

1. TURBT (± intravesical immunotherapy)
   a. Not appropriate—this option is limited to highly selective patients with extensive comorbid disease or poor performance status, and no residual muscle invasive tumor following a re-resection
2. Partial cystectomy

    a. A consideration in selected patients with solitary tumors that are not good radical cystectomy candidates. Not a good choice for this patient with multiple tumors
    b. Renal obstruction is another relative contraindication
3. Bladder-sparing trimodality therapy (aggressive TUR + chemotherapy + radiation)
    a. Requires highly interdisciplinary approach and close follow-up. Not recommended in this patient with multifocal disease
    b. RTOG trials revealed that patients with renal obstruction had inferior outcomes
4. Neoadjuvant chemotherapy followed by radical cystectomy, extended PLND, and urinary diversion—this is the best treatment option for this patient

How do you manage localized muscle-invasive bladder cancer in females (T2a, T2b, T3)?

Perform anterior exenteration.

Organs removed include uterus, ovaries, bladder, urethra, and anterior vaginal wall—although studies suggest that there is a low risk of GYN organ involvement.

Preservation of the vagina and uterus provides support for a neobladder and for the pelvic floor.

What are the indications for neoadjuvant chemotherapy?

Randomized trials show a survival benefit following neoadjuvant chemotherapy (3–4 cycles of Gemcitabine/Cisplatin or 3 cycles of MVAC) in patients with Stage II and III disease.

What modifications can be made in the chemotherapy regimen for patients with renal insufficiency?

Carboplatin and Taxane-based regimens may be substituted for patients with renal insufficiency or other co-morbidities. Efficacy is decreased compared to Cisplatin.

How would the presence of small cell carcinoma affect management recommendations?

Neoadjuvant chemotherapy (similar to chemotherapy for small cell lung cancer) is recommended for patients with any primary small cell carcinoma component in the bladder cancer TUR specimen (Cisplatin/Etoposide).

What is the significance of lymphovascular invasion?

LVI is considered to be an adverse prognostic feature with and increased rate of N+ disease noted a cystectomy.

The patient elects to receive neoadjuvant chemotherapy followed by surgery.

What other factors need to be addressed prior to the initiation of chemotherapy?

1. Unobstruct her left kidney prior to chemotherapy to preserve function
2. Evaluate her left kidney for upper tract UC
3. Determine differential renal function. Should the kidney be salvaged?

She has an obstructed left kidney and a serum Cr of 1.3. Ureteral stent insertion was unsuccessful. A left nephrostomy is placed. An antegrade nephrostogram reveals no suspicious filling defects or tumors. A renogram reveals 40% differential function of left kidney, 60% differential function right kidney. Serum Cr decreases to 0.9.

What is your pre-op work-up?

State that you would obtain informed consent, obtain preoperative labs, administer preoperative antibiotics and DVT prophylaxis. Stop ASA 7 days before surgery.

This patient elects to have a neobladder. She should still see an enterostomal therapist to mark for a potential stoma. To help facilitate bowel recovery following surgery Alvimopan may be considered.

Standard use of an enhanced recovery program after surgery should be considered for cystectomy patients which begin prior to the surgical procedure.

The Operation:

Be prepared to discuss your surgical approach. You are going to perform a cystectomy, an extended pelvic lymph node dissection, and some type of urinary diversion (e.g., Indiana pouch, Florida pouch, neobladder, or ileal conduit).

What are the indications for a urethrectomy (female)?

1. CIS or tumor at the bladder neck or urethra
2. T4 tumor involving the anterior vaginal wall

What are the indications for a urethrectomy (male)?

1. Diffuse CIS of the prostatic urethra or ducts
2. Prostatic stromal invasion
3. CIS or obvious tumor at the urethral/prostatic apical margin

Discuss the principles of orthotopic urinary diversion in females.

1. Cancer at the bladder neck or at the urethra is an absolute contraindication (this patient's bladder neck biopsies were negative)
2. Must preserve the distal urethra and avoid dissection below the endopelvic fascia to prevent damage to the pudendal nerve
3. 15%–20% of women develop hypercontinence and require long term CIC
4. The anterior vaginal wall (and occasionally the uterus and cervix when present) can be preserved to serve as a platform for the neobladder

How would you educate patients regarding daytime and nighttime continence following orthotopic urinary diversions?

1. 80%–90% of patients are continent during the day
2. 55%–65% of patients are continent during the night
3. Continence rates are better for younger (< 65 years) than for older patients (> 65 years)
4. Increased nocturnal incontinence is due to loss of the afferent input from the detrusor to the CNS, which previously resulted in a corresponding increase in the urethral resistance with filling

Describe the surgical technique.

The Operation (Anterior Exenteration—for females)

1. Midline incision
2. Divide urachus
3. Take down lateral pedicles of the bladder
4. Ligate superior vesical artery
5. Divide ovarian vessels (infundibulopelvic ligament)
6. Divide cardinal and uterosacral ligaments
7. Incise the peritoneum in the pouch of Douglas
8. Divide ureters at the level of the bladder
9. Divide urethra at bladder neck and send margin for frozen section analysis

This patient underwent cystectomy with preservation of the anterior vaginal wall and urethra, extended PLND, and orthotopic urinary diversion. There was a small portion of the anterior vaginal wall removed on the left. An omental flap was positioned between the neobladder base and the anterior vaginal wall. Her path stage was T2N0 urothelial carcinoma with mild squamous differentiation and negative surgical margins.

On POD #5, the patient was noted to have increased vaginal drainage. There was no corresponding increase in the abdominal JP drain output.

What is the next step?

Many female patients have vaginal drainage following cystectomy and PLND, especially following vaginal closure. However, increased drainage should raise concern of a neobladder-vaginal fistula.

JP drain fluid and fluid retrieved from the vaginal drainage should be sent for Cr.

Cr on the vaginal fluid was 20.7, serum Cr was 1.0.

How would you evaluate and manage this patient?

1. Consider a gentle cystogram. In this case the study revealed extravasation from a posterior neobladder suture line through the vaginal closure
2. Ensure the Foley is draining adequately and the ureteral stents are unobstructed

All drains are functioning well but on postoperative day #8 the leak persists.

What is the next step in management?

Consider bilateral percutaneous nephrostomies and antegrade nephrostograms. The nephrostograms reveal no extravasation from the ureteral-intestinal anastomoses. By POD #14, the leak subsides. A repeat cystogram 3 weeks post-op reveals no further leak. The stents and the drain are removed followed by the Foley catheter 1 week later.

12 months post-op the patient is doing well—fully continent during the day and only with occasional nocturnal incontinence. Her urine cytology converts to "suspicious for malignancy."

Describe your evaluation.

1. CT urogram	WNL
2. Cystogram	WNL
3. Cystoscopy	papillary tumor at the anterior urethra

She undergoes TUR—path reveals T1 high grade UC. No muscle identified in the resected specimen.

What are your recommendations?

The patient is best served by undergoing an exploration, urethrectomy and conversion of her orthotopic diversion to either a continent catheterizable diversion or an ileal conduit via the afferent limb of the neobladder.

CHAPTER 3

UPPER TRACT UROTHELIAL CARCINOMA

MARLA WARDENBURG, MD
PAUL CRISPEN, MD

CASE 1

HPI: 48-year-old male presents with flank pain and hematuria. Symptoms began 3 weeks ago. He describes the pain as intermittent, radiating from right flank down to groin. Hematuria comes and goes, he denies passing clots. Pain is associated with nausea and one episode of emesis. He denies a history of urinary tract infections and nephrolithiasis.

PMH:	hypertension		
PSH:	none		
Allergies:	none	**Medications:**	Lisinopril
FH:	non-contributory		
SH:	(+) tob, 30-pack year		
ROS:	non-contributory		

PE:

Vitals	T 98.7	BP 136/78	P 88	RR 16
GA	no acute distress			
HEENT	benign			
Heart	RRR			
Lungs	CTA			
Abdomen	soft; NT/ND; (-) mass			
Flank	(+) (R) CVAT			
GU	normal			
Rectal	30 g prostate no nodules			
Ext	(-) CCE			
Neuro	non-focal			

What initial lab tests do you order?

UA	→	10 RBC/HPF;
CBC	→	WBC 8 K/μL; Hgb 14g/dL; Hct 42%; platelets 275 K/mm^3
BMP	→	Na 137 meq/L; K 3.9 meq/L; Cl 108 meq/L; CO2 21 meq/L; BUN 10 mg/dL; Cr 1.2 mg/dL

What is the next step in evaluation/management?

Imaging study of choice is a dedicated CT scan of the abdomen/pelvis with and without IV contrast.

CT scan: Enhancing 2 cm soft tissue mass within (R) distal ureter; marked (R) hydronephrosis, contralateral kidney appears normal; (-) adenopathy or distant metastasis

What is your differential diagnosis?

The differential diagnosis for a ureteral mass includes tumor, fungus ball, blood clot, obstructing papillae, and radiolucent stone. Given the fact that this mass enhances, you are concerned about ureteral urothelial carcinoma (UC).

What is your next step in evaluation?

You need to complete a work-up to:

1. Confirm the diagnosis by obtaining tissue from the lesion
2. Rule out concomitant bladder tumors
3. Rule out metastatic disease

What is your next step in management?

Send off urine cytology, perform cystoscopy with retrograde pyelogram, ureteroscopy, ureteral washings and cold-cup biopsy of the ureteral mass.
You also review the CT scan again and obtain a (preoperative) CXR.
You obtain informed consent and administer preoperative antibiotics.

Urine cytology:	(+) urothelial carcinoma
Ureteral wash:	(+) urothelial carcinoma
Biopsy:	high grade UC
Cystoscopy:	(-) bladder tumor
Ureteroscopy:	2 cm papillary-appearing tumor in distal ureter
CXR:	WNL

What is a standard diagnostic work-up for upper tract urothelial carcinoma (UC)?

1. CT scan of abdomen and pelvis (CT urogram or IVP)
   a. Used to outline filling defects of renal pelvis and calyces
   b. Assess retroperitoneal adenopathy and distant metastasis
2. Cystoscopy
   a. Initial screening for hematuria
3. Retrograde pyelogram
   a. Useful in confirming the presence of filling defects in the renal pelvis and ureter
   b. Is more sensitive than IVP
   c. Can be combined with selective aspiration or barbotaged urine for upper tract cytology
   d. Performed as needed, especially if IVP findings are equivocal
4. Ureteroscopy
   a. Evaluate and biopsy the mass under direct vision
   b. With much improved instrumentation, ureteroscopy with direct visualization of the lesion and biopsy/brushing is becoming the standard of care for confirming the diagnosis of upper tract UC
5. Antegrade pyelography
   a. Risk of tumor spillage at the puncture site
   b. Use only if retrograde procedures fail
6. Nephroscopy
   a. Endoscopic evaluation and management of selected localized low-grade tumors by fulguration and/or resection
   b. Performed as needed

What is your assessment?

48-year-old male with high grade UC of the distal ureter.

What are your treatment options?

1. Nephroureterectomy with cuff of bladder
    a. This is aggressive for what appears to be low volume and stage disease in the distal ureter
    b. Indications for nephroureterectomy with cuff of bladder include normal contralateral kidney and high-grade tumor or uncontrollable local recurrences
        i. High grade ureteral and pelvic tumors unsuitable for local resection should undergo radical surgical extirpation. They may need neoadjuvant or adjuvant chemotherapy
        ii. In cases of uncontrollable local recurrences, nephroureterectomy with cuff of bladder (solitary or bilateral) should be considered. If necessary, renal transplant may be considered after a prudent waiting period of 2 years
2. Segmental resection
    a. Conservative measures (e.g., segmental resection or endoscopic treatment) are indicated when preservation of renal function is mandatory (e.g., low-stage bilateral disease, azotemia, solitary kidney) or low grade lesion
        i. Distal ureteral excision (with removal of bladder cuff) and reimplantation
            aa. This is best option
            bb. He has normal contralateral kidney. Low volume distal ureteral tumors are ideal for ureteral excision and reimplantation
        ii. Primary excision and anastomosis
            aa. The lesion is too distal to allow primary excision anastomosis
            bb. This procedure is best reserved for mid to proximal ureteral tumors
3. Ureteroscopy and resection or fulguration
    a. Although this is an option, you risk ureteral stricture and perforation as well as high rates of recurrence
    b. Endoscopic management is an option for patients with UC in the distal ureter or who are not candidates for major surgery due to medical comorbidities

He agrees to ureteral excision and reimplantation.

How do you proceed?

1. State that you would obtain an informed consent by discussing the surgical procedure, indications, potential risks and complications
2. Discuss option of intravesical mitomycin C immediately after nephroureterectomy
3. Remark that you would obtain pre-operative labs and tests

Describe your surgical technique:

The Operation: Ureteral Excision and Reimplantation (Open or Laparoscopic)

1. Gibson, Pfannenstiel incision, or midline incision if open
2. Identify the ureter as it crosses over the iliac artery
3. Mobilize the ureter to the ureterovesical junction
    a. Removing the tumor
        i. Remove a cuff of bladder around the ureteral orifice
        ii. Cut the distal ureter proximal to the ureteral tumor
        iii. Remove the specimen (ureter-bladder cuff)
        iv. Check ureteral and bladder margins via frozen section
    b. Performing the anastomosis

    i. Prepare and spatulate the ureter
    ii. Create submucosal tunnel
    iii. Close the old hiatus and create a new ureteral orifice
    iv. Suture the ureteral cuff to the bladder mucosa
    v. Insert a stent

4. Close the bladder in anatomic layers
5. Perform ipsilateral pelvic lymph node dissection
6. Leave a pelvic drain and Foley catheter

He underwent distal ureteral excision and reimplantation without complications and was transferred to the recovery room. In the recovery room, he received a 40 mg intravesical instillation of mitomycin C with a dwell time of 1 hour.

What is his post-operative care?

1. Remove the drain when output is minimal
2. Cystogram in 10–14 days
3. Remove Foley when cystogram is normal
4. Discontinue stent in 6 weeks
5. Check his pathology report

Pathology: high-grade UC involving lamina propria; surgical margins negative, nodes negative

What is his pathologic stage?

pT1N0Mx

Discuss the TNM staging system for upper tract TCC:

Upper Tract Carcinoma (AJCC 2010 TNM Stage Classification):

Tx	Primary tumor cannot be assessed
To	No evidence of primary tumor
TIS	Carcinoma in situ
T1	Tumor invades lamina propria; subepithelial connective tissue
T2	Tumor invades muscularis propria of renal pelvis/ureter
T3	Renal pelvis: tumor invades beyond muscularis into peripelvic fat or renal parenchyma Ureter: tumor invades beyond muscularis into periureteric fat
T4	Tumor invades adjacent organs or through the kidney into the perinephric fat
Nx	Nodal involvement unknown
N0	No evidence of nodal involvement
N1	Single node (< 2 cm)
N2	Single node or nodes (2–5 cm)
N3	Single node or nodes (> 5 cm)
Mx	Distant metastasis unknown
Mo	No evidence of distant metastasis
M1	Distant metastasis present

Republished with permission of Springer-Verlag New York Inc, from AJCC Cancer Staging Manual, Edge SB, 7th ed. ©2009; permission conveyed through Copyright Clearance Center, Inc.

Discuss epidemiology of upper tract UC

Upper tract urothelial carcinoma (UTUC) comprises only 5–10% of all UC.
Majority of patients present with higher stage disease compared to bladder UC.
Average age at diagnosis is slightly higher than for bladder UC.
Gender disparity is less compared to bladder UC, with male/female ratio 2:1.

What are clinical signs and symptoms of upper tract UC?

1. Hematuria (gross/microscopic)	60–90%
2. Flank pain	30–40%

3. Constitutional symptoms
   a. Weight loss
   b. Fatigue
   c. Malaise
4. Bone pain

What are potential risk factors for UC of the upper tract?

Most risk factors for UC of the bladder (tobacco, chemical carcinogens, analgesic nephropathy, chronic inflammation/infection) are also risk factors for UTUC.

Risk factors specific to upper tract UC:

1. Balkan nephropathy (Danubian endemic nephropathy)—interstitial nephritis that causes renal insufficiency in people endemic to the Balkan Peninsula
   a. It is thought to arise from consumption of wheat contaminated with aristolochia (a plant toxin)
   b. Patients have a 100–200× risk of UTUC compared to the general population
   c. Aristolochia is also found in some Eastern herbal remedies
2. Lynch syndrome—autosomal dominant DNA mismatch repair syndrome that increases risk of colorectal and endometrial cancer as well as UC
   a. Lifetime risk of upper tract UC is 10–15%
3. Arsenic exposure
4. History of UC of the bladder

What is the relationship between upper tract UC and UC of the bladder?

1. Probability of developing UTUC after bladder UC is about 5%, but 15–20% of patients with UTUC have a history of bladder cancer
2. Risk of UTUC is highest in patients with: History of CIS or high-grade UC
3. History of UC at the UC, trigone, or bladder neck
4. History of multifocal bladder cancer
5. VUR
6. UC at the ureteral margin or distal ureter during cystectomy
7. Probability of developing bladder cancer after upper tract UC ranges 50–70%
8. Probability of developing UC in the contralateral collecting system after upper tract UC ranges 2–5% (higher for patients with Balkan nephropathy or Lynch syndrome)

CASE 2

HPI: 74-year-old female presents with right flank pain and hematuria. Pain started 3 months ago and comes and goes. Hematuria started last month and she was treated for presumed pyelonephritis. She has noted the passage of small blood clots in her urine. The pain will decrease following clot passage. She denies irritative voiding symptoms. She had a mid-urethral sling for stress urinary incontinence 8 years prior. No weight loss.

PMH:
(+) DM
(+) HTN
(+) atrial fibrillation

PSH:
appendectomy
mid-urethral Sling

Allergies: none **Medications:** HCTZ, Pioglitazone, Warfarin

FH: No history of urologic malignancy
SH: (+) tob, 15 pack year, quit 40 years ago; (-) ETOH
ROS: non-contributory

PE:

Vitals	T 98.6	BP 118/54	P 76	RR 14
GA	elderly F; no acute distress			
HEENT	benign			
Heart	RRR			
Lungs	CTA			
Abdomen	soft; no masses; well healed appendectomy scar; no hernias			
Flank	(-) CVAT			
GU	normal female exam			
Ext	(-) CCE; good pedal pulses			
Neuro	non-focal			
Lymph nodes	(-) adenopathy			

ECOG performance status: 2

What initial lab tests do you order?

UA → 10–15 RBC/HPF; (-) WBC
CBC → WNL
BMP → Cr 0.9 mg/dL
Cytology → negative

What is your initial work-up?

State that you would perform cystoscopy in the office and order a CT scan of the abdomen and pelvis (with CT urogram/CT-IVP)

Cystoscopy: normal; with blood from right ureteral orifice
CT scan: (-) retroperitoneal adenopathy;
liver, vena cava, pelvis are normal;

1 cm solid enhancing mass at the (R) mid-pole collecting system, no hydronephrosis

What is your assessment?

74-year-old F with hematuria within (R) mid-pole collecting system mass.

What is your differential diagnosis?

Differential diagnoses for pelvic/ureteral filling defects include radiolucent stone, blood clot, fungus ball, papillary necrosis, tumor, and complex peripelvic cyst. Given the enhancement, you suspect a tumor.

What do you recommend?

Confirm the diagnosis by (R) retrograde pyelogram, ureteroscopy, pyeloscopy, and biopsy of the lesion. The patient agrees to this.

Stop her Warfarin 5 days prior to surgery.

(R) retrograde pyelogram: 1 cm filling defect in right mid pole collecting system

Ureteroscopy and biopsy: superficial appearing papillary tumor on stalk located in mid pole collecting system, no other lesions noted in renal pelvis or ureter; tumor visually removed completely at time of ureteroscopy; non-invasive low-grade UC

What is your assessment?

74-year-old F with upper tract UC.

What is her clinical stage?

Clinical stage TaN0M0.

What are your treatment options?

1. Nephroureterectomy
   a. Traditional treatment for upper tract transitional tumors is total nephro-ureterectomy with excision of bladder cuff
   b. This is may be too aggressive for elderly female with ECOG performance status of 2
2. Segmental resection or local excision
   a. Open pyelotomy with tumor excision and fulguration
   b. Appropriate for selected individuals with low grade, low stage tumors in both kidneys or in a solitary kidney with poor renal function
   c. Not the best option
3. Partial nephrectomy
   a. Reserved for those cases in which renal failure must be avoided
   b. Not the best option
4. Ureteroscopic resection and/or fulguration
   a. If this protocol is chosen, this patient will need a vigilant follow-up with repeated ureteroscopy under general anesthesia

   b. Best reserved for low-grade, low-stage tumors similar to superficial bladder tumors managed by TURBT
   c. Lower morbidity compared to percutaneous approach
   d. Best option for the current patient
5. Percutaneous treatment
   a. Advantage of this approach is facilitation of tumor removal and instillation of anti-tumor medications through nephrostomy tube
   b. Potential risks of this approach include bleeding, tumor spillage, and tumor implantation
   c. Best reserved for those patients with small, solitary tumors not accessible to ureteroscopy
      i. This patient has tumor invading the renal pelvis, and thus percutaneous approach is hazardous
      ii. In the presence of a large aortic aneurysm or if patient is a poor surgical candidate, you may consider percutaneous approach using laser (e.g., YAG or Holmium)
6. Instillation therapy
   a. Best reserved for those patients with multiple superficial tumors or CIS who have compromised renal function or bilateral disease
   b. This patient is relatively healthy and has well-functioning contralateral kidney

She opts for surveillance at this time as the tumor was resected completely endoscopically.

What is your next step in surveillance?

Cystoscopy with right ureteroscopy every 6 months for 3 years then annually thereafter.

Would you recommend any changes in her current medications based upon the new diagnosis of urothelial carcinoma?

Should discuss discontinuing Pioglitazone and starting new antihyperglycemic with her primary care provider. A population based study showed that Pioglitazone, compared with other antidiabetic drugs, is associated with an increased risk of bladder cancer in people with type 2 diabetes.

Are any of her current medications of concern if she developed high grade disease and opt for upper tract instillation therapy with BCG?

Yes, Warfarin therapy has been associated with decreased efficacy of BCG therapy.

CASE 3

HPI: 75-year-old Caucasian male presents to the clinic complaining of painless gross hematuria. Episodes are recurrent for the past 6 months. He denies irritative or obstructive voiding symptoms, and has no history of UTI, nephrolithiasis, or prostatitis. He denies fever/chills, bone pain, fatigue, or unintentional weight loss. He does have a history of cigarette smoking.

PMH:
(+) MI
(+) arrhythmia
(+) HTN

PSH: none
Allergies: none
Medications: ASA QD, Propranolol, Captopril

FH: Mediterranean descent
SH: (+) tob, 25 pack year; (-) ETOH
ROS: non-contributory

PE:

Vitals	T 98.6	BP 160/60	P 90	RR 12
GA	elderly CM INAD			
HEENT	benign			
Heart	RRR			
Lungs	CTA			
Abdomen	soft;			
Flank	(-) CVAT			
GU	normal circumcised phallus; adequate meatus; (B) testicles WNL			
Prostate	smooth and benign @ 30 g; (-) nodules or induration			
Ext	(-) CCE; good pedal pulses			
Neuro	non-focal			
Lymph nodes	(-) adenopathy			

What initial lab tests do you order?

UA → 10–15 RBC/HPF; (-) WBC
CBC → WNL
BMP → Cr 1.2 mg/dL
Cytology → (+) UC

What is your initial work-up?

State that you would perform cystoscopy in the office and order a CT scan of the abdomen and pelvis (with CT urogram/CT-IVP).

Cystoscopy: normal; no bleeding from either ureteral orifice
CT scan: (-) retroperitoneal adenopathy;
liver, vena cava, pelvis are normal;
4 cm solid enhancing mass at the (R) lower pole collecting system

What is your assessment?

75-year-old CM with enhancing mass/filling defect within (R) lower pole collecting system.

What is your differential diagnosis?

Differential diagnoses for pelvic/ureteral filling defects include radiolucent stone, blood clot, fungus ball, papillary necrosis, tumor, and complex peripelvic cyst. Given the enhancement, you suspect a tumor.

What do you recommend?

Confirm the diagnosis by selective cytology, (R) retrograde pyelogram, ureteroscopy, pyeloscopy, and biopsy of the lesion. The patient agrees to this.

Stop his ASA 7 days prior to his surgery.

(R) retrograde pyelogram:	goblet sign at UPJ area; large filling defect
Ureteral cytology:	non-diagnostic
Ureteroscopy and biopsy:	high-grade UC with invasion of renal pelvis

What is your metastatic work-up?

State that you would obtain CXR. In addition, consider liver function tests to stage his tumor.

CXR → WNL
LFTs → WNL

What is your assessment?

75-year-old CM with upper tract UC.

What is his clinical stage?

Clinical stage T2N0M0.

What are your treatment options?

1. Nephroureterectomy (+/- neoadjuvant chemotherapy)
   a. Traditional treatment for upper tract transitional tumors is total nephron ureterectomy with excision of bladder cuff
   b. If bladder cuff is not excised, there is 30–75% incidence of tumor recurrence in the ureteral stump
   c. Best protocol for this patient with high-grade invasive UTUC
2. Segmental resection or local excision
   a. Open pyelotomy with tumor excision and fulguration
   b. Appropriate for selected individuals with low grade, low stage tumors in both kidneys or in a solitary kidney with poor renal function

   c. Recurrence rates following conservative excision are higher than those following local resection of ureteral tumors. The tumor recurrence rate after local excision renal pelvis tumor range from 25–40%
   d. Not the best option
3. Partial nephrectomy
   a. Should be reserved for those cases in which renal failure must be avoided
   b. Local tumor recurrence with this approach is 38%
   c. It is technically challenging to perform a partial nephrectomy on a tumor situated at the ureteropelvic junction. In addition, he has normally functioning contralateral kidney
   d. Not the best option
4. Ureteroscopic resection and/or fulguration
   a. If this protocol is chosen, this patient will need a vigilant follow-up with repeated ureteroscopy under general anesthesia
   b. Best reserved for low-grade, low-stage tumors similar to superficial bladder tumors managed by TURBT
   c. This is not the best option
5. Percutaneous treatment
   a. Advantage of this approach is facilitation of tumor removal and instillation of anti-tumor medications through nephrostomy tube
   b. Potential risks of this approach include bleeding, tumor spillage, and tumor implantation
   c. Should be reserved for those patients with small, solitary tumors not accessible to ureteroscopy. This patient has tumor invading the renal pelvis, and thus percutaneous approach is hazardous. In the presence of a large aortic aneurysm or if he is a poor surgical candidate, you may consider percutaneous approach using laser (e.g., YAG or Holmium)
6. Instillation therapy
   a. Should be reserved for those patients with multiple superficial tumors or CIS who have compromised renal function or bilateral disease; this patient is relatively healthy and has well-functioning contralateral kidney
7. Radiation therapy
   a. Radiation is best used for local control of tumor and should be used as adjuvant or palliative therapy for high-grade or invasive lesions; this is not indicated at this time
8. Angioinfarction
   a. Rarely used for treatment of upper tract tumors
   b. May have a role for those symptomatic patients with incurable distant metastasis or those who are not candidates for nephrectomy
   c. This patient has localized tumor and is a good surgical candidate; angioinfarction is not indicated

He opts for neoadjuvant chemotherapy with nephroureterectomy with excision of bladder cuff.

Discuss the rationale for neoadjuvant chemotherapy for upper tract UC.

Many patients are renally impaired after nephroureterectomy and lose eligibility for Cisplatin-based chemotherapy after surgery.

The lower incidence of UTUC has made it difficult to perform prospective clinical trials and much is extrapolated from studies of neoadjuvant chemotherapy for bladder cancer.

However, 2 recent retrospective studies have shown significant down-staging before surgery and increased 5-year overall survival after neoadjuvant chemo and nephroureterectomy compared to surgery alone (80% vs 57.6%) for high-risk UTUC.

Chemotherapy regimens (Gemcitabine/Cisplatin or MVAC) are similar to those for bladder UC.

The patient tolerates 4 cycles of chemotherapy without complication and minimal change in renal function.

How would you prepare this patient for nephroureterectomy?

1. State that you would obtain an informed consent by discussing the surgical procedure, indications, potential risks, and complications
2. Remark that you would obtain preoperative labs and tests
3. Discuss option of intravesical Mitomycin C immediately after nephroureterectomy
4. In addition you would bowel prep this patient and place sequential compressive devices (SCD)

Describe your surgical technique:

The Operation (Nephroureterectomy)

I. Radical nephrectomy (open or laparoscopic)
    1. Transperitoneal or retroperitoneal approach
    2. On (L) side reflect the colon medially and divide splenocolic ligament
        a. Ligate and divide gonadal and adrenal vein
        b. Ligate and divide renal artery and vein
        c. Mobilize the kidney
    3. On (R) side, perform Kocher maneuver
        a. Ligate and divide renal artery and vein
        b. Mobilize the kidney

II. Excision of bladder cuff
    1. Gibson or midline incision if open
    2. Identify the ureter as it crosses over the iliac artery
    3. Mobilize the ureter to the ureterovesical junction
    4. Remove a cuff of bladder around the ureteral orifice
    5. Remove the specimen (kidney-ureter-bladder cuff)
    6. Close the bladder in anatomic layers
    7. Leave a pelvic drain and Foley catheter

You also did a limited lymph node dissection.

Operation is uncomplicated and he is transferred to the recovery room.

What is the role of intravesical chemotherapy after nephroureterectomy?

A single post-operative dose of Mitomycin C immediately after nephroureterectomy for UTUC has been shown to decrease risk of developing UC of the bladder (relative risk reduction 40% compared to surgery alone). The number needed to treat based upon a randomized clinic trial was 9.

What is his post-operative care?

1. Remove the drain when output is minimal
2. Cystogram in 10–14 days
3. Remove Foley when cystogram is normal
4. Check his pathology report

Pathology report: High grade UC invading the renal parenchyma; 3 lymph nodes negative

What is his pathologic stage?

pT3N0M0

What do you recommend?

No additional adjuvant therapy is indicated at this time. He must undergo close surveillance of the bladder and contralateral upper tract.

Cystoscopy	Q 3 mo × 2 yrs, Q 6 mo × 2 yrs, then Q yr
Cytology	Q 3 mo × 2 yrs, Q 6 mo × 2 yrs, then Q yr
CT scan or IVP	Q 3–6 mo × 2 yrs, then less often
CXR	Q 6 mo × 2 yrs, then less often

CHAPTER 4

PENILE CARCINOMA

GREGORY J DIORIO, MD
PHILIPPE E. SPIESS, MD

CASE 1

HPI: 65-year-old African-American male with penile lesion for 1 year. Has minimal lower urinary tract symptoms. AUA Sx score is 5/35.

PMH: glaucoma; HTN; NIDDM; hypercholesterolemia; (-) STDs

PSH: none

Allergies: none **Medications:** Lasix, Lipitor, Glyburide

FH: (-) prostate cancer
SH: (-) tob; (-) ETOH; retired
ROS: non-contributory

PE:

Vitals	T 98.6	BP 140/60	P 90	RR 12
GA	WDWN AAM INAD			
HEENT	benign			
Heart	RRR			
Lungs	CTA			
Abdomen	mild obese; soft; NT/ND			
Flank	benign			
GU	uncircumcised phallus; adequate meatus; 2 cm fungating mass inner prepuce; (B) testicles WNL			
Prostate	smooth and benign @ 30 g			
Lymph nodes	(bilateral) inguinal adenopathy, mobile, <4 cm			
Ext	(-) CCE			
Neuro	non-focal			

What initial lab tests do you order?

UA → WNL
UCx → no growth
Chem 7 → WNL
CBC → WNL

What is your differential diagnosis?

1. Squamous cell carcinoma of the penis
2. Verrucous carcinoma (Buschke-Löwenstein tumor)
3. Condyloma acuminata

How does penile carcinoma present?

1. Penile mass (50%)
2. Sore or ulcer on penis (35%)
3. Phimosis
4. Irritative/Obstructive voiding symptoms

What are systemic symptoms of penile carcinoma?

1. Weakness
2. Weight loss

3. Malaise
4. Fatigue

How do you make the diagnosis of penile carcinoma?

You must obtain tissue biopsy.

Prepuce → Excisional biopsy with circumcision
Glans → Excisional biopsy including margin to assess invasion
Shaft → Excisional biopsy including margin to assess invasion

What do you do next?

Excisional biopsy of the penile mass.

Pathology: squamous cell carcinoma; invasion into corpus cavernosum

What is your assessment?

65-year-old AAM with newly diagnosed penile cancer.

What is your next step?

This patient needs metastatic work up and clinical staging.

CXR → normal
CT scan (abd and pelvis) → (+) inguinal adenopathy; (-) retroperitoneal adenopathy; (-) pelvic adenopathy

Note: While most patients with a diagnosis of penile cancer are staged with a CT scan abdomen/pelvis, only patients with positive inguinal nodes have a strong indication for this study. CT and MRI are limited in patients with non-palpable disease. MRI appears to be the best choice in patients where examination of the inguinal region is difficult (obesity, previous inguinal chemotherapy/radiation, surgery).

LFTs → WNL
Serum calcium → WNL

Note: Hypercalcemia in the absence of detectable osseous metastasis has been noted. Hypercalcemia appears to be a function of bulk of the disease. It is often associated with inguinal metastasis and may resolve with inguinal lymphadenectomy.

What is minimal diagnostic evaluation for penile carcinoma?

1. Primary tumor
    a. Physical examination
    b. Tissue biopsy
    c. If extensive local invasion, i.e., of corpus cavernosum, is suspected: MRI
2. Regional lymph nodes
    a. Physical examination
    b. CT scan if clinically indicated (high risk patients and those who cannot be diagnosed by clinical exam)
    c. If nodes remain palpable: tissue diagnosis
3. Distant metastasis
    a. CXR

b. CT scan
c. Bone scan (optional; main indication is in symptomatic patients)
d. FDG-PET/CT Scan (optional for evaluation of metastatic disease)
e. LFTs and serum calcium

What is his clinical stage?

Clinical stage T2cN2Mx penile cancer with possible inguinal metastasis.

What are other important prognosticators aside from tumor stage?

1. Lymph node status (most important prognostic indicator)
2. Tumor grade
3. Presence of lymphovascular invasion

What is your recommendation?

Perform partial penectomy.

First thing to do is to remove the primary lesion. He needs partial penectomy with a negative margin. Studies have shown that surgical margins of 5–10 mm are as safe as traditional 2 cm margins, and 10–20 mm margins provide adequate tumor control.

If a negative margin cannot be obtained or if the penile shaft is too short for the patient to void standing up, you must proceed with total penectomy combined with perineal urethrostomy.

How do you proceed?

You obtained informed consent for partial penectomy; you should also obtain consent for possible total penectomy and perineal urethrostomy if partial is not feasible.
Obtain preoperative labs, and give him preoperative antibiotics.

Discuss your surgical technique:

The Operation (Partial Penectomy):

1. Minimize contamination from the tumor
2. Wrap a glove or sponge around the distal penis
3. Place an occluding tourniquet at the base of penis to minimize blood loss
4. Make a circumferential incision 2–3 cm proximal to tumor
5. Carry incision down to Buck's fascia
6. Ligate neurovascular bundles
7. Mobilize urethra and corpus spongiosum from corpora cavernosa
8. Transect the urethra but allow it to protrude slightly from the penile shaft
9. Transect and suture-ligate each corpus cavernosum
10. Evert and suture the urethral margins to the skin
11. Insert Foley catheter

He tolerated the procedure well and was discharged to home.

What is your follow-up?

In patients with clinically palpable lymph nodes, the likelihood of metastatic nodal disease is very high, and the traditional treatment of a prolonged course of antibiotics to exclude inflammatory disease is no longer recommended. If cellulitis is clinically present antibiotics may be indicated prior to intervention. You also need to check his pathology.

Pathology: pT2cN2Mx

What are the consequences of untreated metastatic inguinal adenopathy?

1. Distant metastatic spread
2. Local invasion with skin necrosis
3. Infection
4. Sepsis
5. Hemorrhage from erosion into femoral vessels
6. Death from exsanguination

You need to know how to manage the following scenarios:

1. Non palpable inguinal nodes
2. Palpable inguinal lymph nodes (<4 cm, unilateral or bilateral and mobile)
3. Palpable inguinal lymph nodes (>4 cm, multiple, fixed)

Discuss the management of inguinal lymph nodes for clinical stages Tis, Ta, T1-3, N1-3, M0.

1. Non-palpable Inguinal Nodes
    a. Low risk group (pTis, pTa or pT1a)
        i. Risk of occult metastases is less than 15%
        ii. Close, active surveillance
        iii. If patient unreliable, consider dynamic sentinel lymph node biopsy (DSLNB)
    b. Intermediate risk group (pT1b)
        i. Active surveillance in reliable patients without evidence of vascular or lymphatic invasion or in select patients who are compliant with vigorous follow up
        ii. Modified bilateral superficial inguinal node dissection with frozen section
        iii. If any nodes are positive, perform standard (superficial and deep) ilioinguinal lymph node dissection (ILND) on that side
        iv. Consider DSLNB in select patients
    c. High risk group (pT2 or G3)
        i. Risk of occult metastases up to 70%
        ii. Modified bilateral (or standard) inguinal node dissection with frozen section. If any nodes are positive, perform standard (superficial and deep) ilioinguinal lymph node dissection on that side
2. Inguinal nodes become palpable on one side
    a. See treatment for palpable nodes
    b. Unilateral palpable inguinal node (<4 cm): Perform bilateral superficial ILND (or radical) with standard ILND (superficial and deep) on ipsilateral side
    c. If contralateral positive on frozen section, proceed with standard (superficial and deep) ILND
3. Multiple, >4 cm fixed inguinal nodes, + pelvic nodes
    a. Neoadjuvant chemotherapy
    b. Consolidative surgery if clinical response
    c. Proceed with pelvic lymph node dissection if >2 inguinal nodes positive on frozen section or in delayed procedure in patients with extranodal extension

Your patient asks you what you intend to do with his bilaterally enlarged lymph nodes. He is extremely concerned they may harbor cancer.

How do you proceed?

He needs bilateral ILND with intraoperative frozen sections.

1. State that you would obtain an informed consent by discussing the surgical procedure, indications, potential risks and complications
2. Remark that you would obtain preoperative labs and tests
3. In addition you would anticoagulate this patient and place sequential compressive devices (SCD)
4. Measure for Jobst stockings 1 week before surgery

Labs: → Chem 7, CBC, PT/PTT
Tests: → CXR, EKG
Blood: → T&C, autologous, or cell saver
SCDs: → place before induction of anesthesia
IV antibiotics: → 1 hour before surgery

Discuss the limits of ILND:

1. Modified dissection
   a. Excludes area lateral to the femoral artery and caudal to the fossa ovalis with preservation of the saphenous vein and elimination of need to transect Sartorius muscle to decrease morbidity associated with standard ILND
   b. Empty space

   Note: Remember the mnemonic NAVEL: nerve, artery, vein, empty space, lymphatics. The premise is to remove the **superficial** cluster of lymph nodes around the sapheno-femoral junction above the fascia lata.

2. Standard dissection
   a. Femoral triangle
      i. Lateral boundary → sartorius muscle
      ii. Medial boundary → adductor longus
      iii. Base of the triangle → inguinal ligament (Poupart's ligament)
      iv. Apex of the triangle → apex of femoral triangle
   b. Sartorius flap—Sartorius muscle is detached from anterior iliac spine to cover up the femoral vessels

Note: The idea is to remove the cluster of lymph nodes around the sapheno-femoral junction above and below the fascia lata.

IMPORTANT: The node of Cloquet or Cabanas' sentinel node is totally unreliable and should not be performed.

What are the complications of ILND?

1. Skin slough
   a. Flap necrosis is common because of insufficient subcutaneous tissue
   b. To avoid this, a thick skin flap should be raised using atraumatic technique
   c. Viability of the flap depends on the anastomotic vessels that run in the Camper's fascia
2. Infection
   a. Wound infection and seromas may occur in devascularized areas and dead spaces
   b. This is avoided by proper surgical technique, gentle handling of tissues, appropriate use of closed suction drains and antibiotics
3. Bleeding
   a. Bleeding from the femoral vessels is rare
   b. If the skin flap is too thin and necrotic, arterio-cutaneous or veno-cutaneous fistula may develop in the absence of Sartorius muscle interposition

4. Lymphocele
    a. Lymphocele may be prevented by ligating all lymphatics and tacking the skin flap down to the muscle
    b. Because the lymphatic drainage of the penis to the groin runs in Camper's fascia, this layer should be preserved and left attached to the skin flap
5. Nerve injury
    a. Femoral nerve injury is rare
    b. Proper identification and preservation of femoral nerve should assure its anatomic and functional integrity
6. DVT
    a. Postoperative immobilization is a risk factor for DVT formation
    b. Pneumatic compression boots and early cautious ambulation should prevent occurrence of DVT
    c. Although anticoagulation may be used, realize the risk of lymphocele
7. Lymphedema
    a. Postoperative use of Jobst stockings (elastic stockings) should minimize leg edema
    b. Feet should be elevated when sitting down or lying in bed

When do you perform pelvic lymph node dissection?

Proceed with PLND if any positive pelvic lymph nodes, >2 inguinal nodes are positive for malignancy on frozen section or presence of extranodal extension on final pathology.

What is the lymphatic drainage of the penis?

1. Prepuce and penile skin → superficial inguinal nodes (nodes above the fascia lata)
2. Glans, urethra, corpora → superficial inguinal nodes; deep inguinal nodes (nodes below the fascia lata); pelvic nodes (external iliac, internal iliac, obturator)

Note: Squamous cell carcinoma spreads via lymphatic system. Lymphatic drainage of the penis crosses the midline.

What are prognostic factors of survival for penile carcinoma?

1. Number and site of positive nodes
2. Tumor stage and grade
3. Size of the primary tumor
4. Presence of extranodal extension

What types of cancers arise from the penis?

1. Squamous cell carcinoma (95%)
    a. Most common
    b. Aggressive
    c. Need inguinal lymph node dissection
2. Basal cell carcinoma
    a. Rare
    b. Wide local excision is curative
3. Melanoma
    a. Rare
    b. two-thirds occur on glans

   c. Carries poor prognosis
   d. Surgery is primary therapy
   e. Radiation, chemotherapy and immunotherapy are adjunctive and palliative
4. Kaposi's sarcoma
   a. Only 50% malignant
   b. Must biopsy before treatment
   c. Perform wide local excision and partial penectomy
   d. Inguinal lymph node dissection not needed unless adenopathy is palpable

Where do metastatic tumors to the penis originate?

1. Prostate
2. Bladder
3. Rectum

Note: Symptoms of metastatic tumors include priapism and local swelling.

Discuss the TNM staging system for penile cancer:

Penile Cancer (AJCC 7th edition TNM Stage Classification):

Tx	Cancer stage unknown
To	No evidence of cancer
Tis	Carcinoma in situ
Ta	Verrucous carcinoma (non-invasive)
T1a	Tumor invades subepithelial connective tissue and is not poorly differentiated
T1b	Tumor invades subepithelial connective tissue and is poorly differentiated
T2	Tumor involves corpus cavernosum or spongiosum
T3	Tumor invades urethra or prostate
T4	Involvement of adjacent structures
cNx	Regional lymph nodes cannot be assessed
cNo	No evidence of nodal involvement
cN1	Palpable mobile unilateral lymph node
cN2	Palpable mobile multiple or bilateral lymph nodes
cN3	Palpable fixed inguinal nodal mass or pelvic lymphadenopathy unilateral or bilateral deep inguinal or pelvic lymph nodes (unilateral or bilateral)
pNx	Regional lymph nodes cannot be assessed
pN1	Metastasis in a single inguinal node
pN2	Metastasis in multiple or bilateral lymph nodes
pN3	Extranodal extension of lymph nodes or pelvic lymph node(s) unilateral or bilateral
Mx	Distant metastasis unknown
Mo	No evidence of distant metastasis
M1	Distant metastasis present

Republished with permission of Springer-Verlag New York Inc, from AJCC Cancer Staging Manual, Edge SB, 7th ed. ©2009; permission conveyed through Copyright Clearance Center, Inc.

CASE 2

HPI: 45-year-old blind African-American male with penile ulcer for unknown length of time. Has minimal lower urinary tract symptoms and he thinks he can empty his bladder well.

PMH: none

PSH: none

Allergies: none **Medications:** Bacitracin ointment

FH: (-) prostate cancer
SH: (+) tob; (+) ETOH
ROS: non-contributory

PE:

Vitals	T 98.6	BP 140/60	P 90	RR 12
GA	WDWN AAM INAD			
HEENT	blind in both eyes; otherwise benign			
Heart	RRR			
Lungs	CTA			
Abdomen	soft; NT/ND			
Flank	benign			
GU	circumcised phallus; 2 cm oval ulcer with firm and raised edges at the glans penis; floor of the ulcer is red; ulcer is indurated and tender; the entire glans penis feels firm and indurated (B) testicles WNL			
Prostate	smooth and benign @ 30 g			
Lymph nodes	No palpable lymphadenopathy			
Ext	(-) CCE			
Neuro	non-focal			

What initial lab tests do you order?

UA → WNL
UCx → no growth
Chem 7 → WNL
CBC → WNL
FTA-Ab test → negative
Dark field exam → negative

What is your differential diagnosis?

1. Erythroplasia of Queyrat
2. Chancre
3. Chancroid
4. Circinate balanitis (Reiter's disease)
5. Penile carcinoma

What are the risk factors for penile carcinoma?

1. Phimosis

2. Chronic irritation related to poor hygiene (BXO)
3. Human papilloma virus (type 16 and 18)

Is circumcision protective against development of penile carcinoma?

1. Penile carcinoma is rare in neonatally circumcised men
2. Incidence of penile carcinoma is higher when circumcision is delayed after puberty
3. Adult circumcision has no protective effect against penile carcinoma

What are pre-cancerous lesions (penile intraepithelial neoplasia (pTis) of the penis and the glans?

1. Erythroplasia of Queyrat (CIS)
    a. Occur on glans penis
    b. 20% progress to invasive cancer
2. Bowen's disease (CIS)
    a. Occur on shaft of penis
    b. 50% will progress to invasive cancer

What are treatment options for pTis?

1. Laser therapy (CO_2 or Nd-YAG)
2. Cryotherapy
3. Photodynamic therapy
4. Topical imiquimod (Aldara)
5. 5-FU cream
6. Local excision
7. Moh's surgery

Note: The objective of treatment in pTis is surgical cure while preserving the penis.

Your patient wants to know what you are going to do for his penile ulcer.

How do you respond?

You recommend excisional biopsy of the glandular mass. He agrees.

How do you proceed?

You obtain informed consent and perform the biopsy.

He tolerates the procedure well and is discharged to home.

What is your next step?

Ask for the pathology report.

Pathology: squamous cell carcinoma; moderately differentiated; invasion of the corpus cavernosum

What is your assessment now?

45-year-old AAM with newly diagnosed penile cancer.

What is your next step?

This patient needs metastatic work up and clinical staging.

CXR → normal

CT scan (abd and pelvis) → (+) right inguinal adenopathy; (-) retroperitoneal adenopathy (-) pelvic adenopathy

LFTs → WNL (indicated in patients with suspected metastatic disease)

Bone scan → negative (indicated in patients with systemic disease and relevant symptoms)

MRI of penis → invasion of corpus cavernosum; distal corpus spongiosum and urethra are also involved (only indicated when considering Penile Sparing Surgery to determine depth/extent of invasion)

What is his clinical stage?

Clinical stage T2cN0Mx penile cancer.

What are important parameters when assessing the clinical nodal status in patients with penile carcinoma?

1. Diameter of node(s) or masses
2. Unilateral or bilateral location
3. Number of nodes identified in each inguinal area
4. Mobile or fixed nodes or masses
5. Relationship to other structures (e.g., skin, Cooper's ligament) with regards to infiltration, perforation
6. Presence of edema on leg and/or scrotum

What are the risk categories for developing nodal metastasis?

Low risk: pTis, pTaG1-2 or pT1a
Intermediate risk: pT1b
High risk: pT2 or higher

What is your initial treatment?

Penile sparing surgery or penectomy (partial or total).

If the lesion is amenable to penile sparing surgery, consider wide local excision, partial or total glansectomy with split thickness skin graft, glans resurfacing, Moh's micrographic surgery, laser, 5FU, or radiation.

How do you proceed?

You obtained informed consent, preoperative labs, and gave him perioperative antibiotics. You also discussed with him the possibility of proceeding with total penectomy in the event you could not perform partial penectomy.

Your partner attempted to do partial penectomy but could not obtain adequate proximal margin. So you proceeded with total penectomy and urethrostomy.

Discuss your surgical technique:

The Operation (Total Penectomy)

1. Exclude the tumor from the field as discussed for partial penectomy
2. Make a circumscribing incision around the base of the penis
3. Mobilize the urethra at the penoscrotal junction
4. Transect the urethra and mobilize it toward the GU diaphragm
5. Divide and ligate neurovascular bundles
6. Divide and suture-ligate corporal bodies
7. Leave a drain
8. Close the incision

The Operation (Perineal Urethrostomy)

1. Dorsolithotomy incision
2. Vertical incision in the perineum
3. Split the bulbocavernosus muscles
4. Mobilize the urethra and bring out through the perineal incision
5. Spatulate and evert the urethra
6. Sew the urethra to the perineal skin
7. Insert Foley catheter

He tolerated the procedure well and was discharged to home.

What is your follow-up?

You need to check his pathology.

Pathology: poorly differentiated squamous cell carcinoma; invasion of both corporal bodies; distal corpus spongiosum and urethra are also involved; pT3NxMx

His inguinal lymph nodes remain nonpalpable.

How do you proceed?

Your partner recommended fine needle aspiration (FNA) of his inguinal lymph node.

FNA: atypical cells; suspicious for malignancy

Is FNA a reasonable approach?

You may attempt FNA of clinically palpable inguinal nodes or pelvic lymph nodes seen on CT scan. The problem with FNA is that a negative FNA does not necessarily rule out LN metastases.

All positive results should be confirmed with excisional biopsy. In the case of negative FNA and clinically suspicious nodes, repeat biopsy or schedule for formal node dissection.

What is your next recommendation?

He has clinical T3 N+ disease and needs ipsilateral standard ILND and contralateral modified ILND (standard if any nodes positive on frozen section) with possible (B) PLND if ILND is positive.

How do you manage non-palpable inguinal lymph nodes in patients with pTis, pTa, or pT1a disease?

1. Risk of occult metastases is less than 15%
2. Close, active surveillance
3. If patient unreliable, perform modified inguinal node dissection frozen section or DSLNB

How do you manage non-palpable inguinal lymph nodes in patients with pT1b?

1. Active surveillance in reliable patients without evidence of vascular or lymphatic invasion
2. All others: modified bilateral inguinal node dissection with frozen section
3. If unilateral nodes positive, perform standard (superficial and deep) ILND, and contralateral modified (superficial) IILND

How do you manage non-palpable inguinal lymph nodes in patients with pT2 or higher disease?

1. Risk of occult metastases up to 70%
2. Modified bilateral (or radical) inguinal node dissection
3. If any nodes positive, proceed with standard ILND

How do you manage palpable inguinal lymph nodes at presentation?

Ipsilateral standard IILND (superficial and deep); contralateral modified ILND

He agrees to lymph node dissection.

How do you proceed?

1. State that you would obtain an informed consent by discussing the surgical procedure, indications, potential risks and complications
2. Remark that you would obtain preoperative labs and tests
3. In addition you would anticoagulate this patient and place sequential compressive devices (SCD)
4. Measure for Jobst stockings 1 week before surgery

Labs: → Chem 7, CBC, coags
Tests: → CXR, EKG
Blood: → T&X, autologous, or cell saver
SCDs: → place before induction of anesthesia
IV antibiotics: → 1 hour before surgery

What type of skin incision do you make?

1. PLND—infra-umbilical vertical midline
2. ILND—curved or elliptical incision 2-fingerbreadths below the inguinal ligament

He underwent (R) ILND, and intraoperative frozen section was positive for metastatic squamous cell carcinoma.

Now what do you do?

Perform contralateral superficial ILND.

When do you perform pelvic lymph node dissection?

Proceed with PLND if the >2 ilioinguinal nodes are positive for malignancy, or presence of extranodal extension on pathology.

Both inguinal lymph nodes and pelvic lymph nodes were positive for metastatic squamous cell carcinoma.

What is his clinical stage?

Clinical stage pT3N3Mx.

What is your recommendation?

Oncology consult for adjuvant chemotherapy.

What are the chemotherapy regimens used in squamous cell carcinoma of the penis?

1. Paclitaxel, Ifosfamide and Cisplatin
2. Cisplatin and 5-FU
3. Vincristine, Methotrexate and Bleomycin

Does presence of inguinal adenopathy mean the patient has inguinal metastasis?

Of men with penile carcinoma, 50% will have palpable adenopathy at presentation.

1. Of these, 30–50% are due to local inflammation
2. Of these, 50% will have cancer

What is the incidence of micrometastasis in clinically negative inguinal nodes?

In presence of clinically negative nodes, 20% will have micro metastasis.

1. Stage I will have 11% micro metastasis
2. Stage II will have 60% positive nodes

Why do you have to evaluate both groins?

Penile lymphatics cross the midline, necessitating bilateral evaluation.

When does most microscopic inguinal metastasis become apparent?

Most inguinal metastasis becomes apparent within 2–3 years of initial diagnosis.

Is ilioinguinal lymph node dissection therapeutic?

Yes, ilioinguinal node dissection is therapeutic. The 5-year survival rate is 50% for patients with positive ilioinguinal nodes who have had completely resected inguinal nodes.

If pelvic lymph nodes are positive, what does this mean?

Pelvic lymph node involvement indicates distant metastatic disease and carries a very poor prognosis.

How do you manage recurrent disease in the inguinal region?

1. Recurrence in the inguinal region caries a poor prognosis (median survival < 6 months)
2. Salvage options include surgery, systemic chemotherapy and radiation therapy
3. Salvage ILND has been proven to be beneficial in the patients (preferred)
4. Increased risk of morbidity and post-operative complications

Discuss the role of radiation therapy in the treatment of penile cancer.

1. Effective treatment for primary tumor (>T1) can use External Beam Radiotherapy, brachytherapy or combination
2. Higher recurrence rates when compared to surgery
3. Not recommended as primary treatment of inguinal nodal disease

What is the efficacy of systemic chemotherapy for metastatic penile carcinoma?

The efficacy of systemic chemotherapy is limited. The decision to treat should be individualized based on the patient's age, performance status and preference. Both extending survival and palliation/quality of life are acceptable indications. The most commonly used combinations include:

1. Cisplatin based regimens (Paclitaxel, Ifosfamide and 5-FU)
   a. Overall response rate: approximately 30%
2. Cisplatin, Bleomycin and Methotrexate
   a. Overall response rate: approximately 30%
   b. Up to 10% treatment-related deaths
   c. Bleomycin is not recommended due to high toxicity

CHAPTER 5

PROSTATE CARCINOMA

SAMAY JAIN, MD

CASE 1

HPI: 65-year-old African-American male referred from his primary care physician with a PSA elevated to 8.1ng/mL. He has minimal lower urinary tract symptoms with an IPSS of 6 and has good potency with a SHIM of 22. If not given, make sure that you elicit the patient's performance status. His ECOG is 0.

PMH: HTN, hypercholesterolemia

Allergies: none **Medications:** Lisinopril, Lipitor

FH: negative for prostate cancer
SH: (-) tob; (-) ETOH; history of cocaine abuse; appendectomy > 20 years ago
ROS: (+) for some muscle pains; (-) for bone/back pain, weight loss, hematuria

PE:

Vitals	T 98.6	RR 12	BP 135/86	BMI 30
GA	WDWN, AAM, INAD			
HEENT	WNL			
Heart	RRR, no MRG			
Lungs	CTA B			
Abdomen	soft; non-tender; non-distended; no masses			
GU	circumcised; penis, glans, scrotum, testicles all normal			
DRE	normal rectal tone; prostate is smooth, slightly larger on the right, no nodules, the borders are distinct and it is approximately 40 g			
Ext	no edema			
Neuro	non-focal			

What tests would you order?

UA → normal

What is your assessment?

65-year-old AAM with elevated PSA.

What is your differential?

1. Enlarged prostate (BPH)
2. Urinary tract infection
3. Prostatitis
4. Prostate cancer

What are the management strategy options that you would present this patient?

1. Observation with repeat PSA
2. Prostate MRI—controversial, be willing to defend this with data supporting its use pre-biopsy
3. Prostate biopsy

You and your patient elect for a prostate biopsy.

Review informed consent for a prostate biopsy.

In general, informed consent should review all of the reasonable alternatives to the recommended procedure as well as the risks and expected benefits of the procedure. The risks of anesthesia, if applicable, should be reviewed as well.

For this particular case, the alternative is observation with a repeat PSA, which carries a risk of a missed diagnosis and potential delay in treatment.

Risks of transrectal ultrasound guided prostate biopsy (TRUSPB) include: pain/discomfort, UTI, urinary retention, hematuria, hematospermia, hematochezia, sepsis and death. There is data to support that some men will experience transient erectile dysfunction following TRUSPB.

How would you prepare for his biopsy?

Ensure that patient is off all blood thinners.

Perform a rectal swab for Fluoroquinolone resistant organisms—this was recommended by the AUA QI Summit in 2014, but has not been included in any definitive, wide spread guidelines.

Review the AUA best practice guidelines for antimicrobial prophylaxis

Based on the AUA best practice guideline, you should prescribe the patient a single dose or single day dose of a Fluoroquinolone or 1st/2nd/3rd generation Cephalosporin as a first choice or TMP/SMX or an Aminoglycoside as an alternative. A single dose or single day dose has been shown to be as effective as 3-day dosing and is now the preferred dosing schedule.

You elect to perform a rectal swab looking for Cipro resistant E Coli/organisms—this shows all flora are Ciprofloxacin sensitive E. coli.

You treat the patient with a one-time dose of 500mg PO Cipro prior to his biopsy.

How does Ciprofloxacin work and what are its side effects?

Fluoroquinolones work by inhibiting DNA gyrase and the side effects are a risk of allergic reaction and tendonitis and tendon rupture. They may exacerbate muscle weakness in patients with myasthenia gravis.

Note: In general be sure to understand the mechanism of any medication you order as well as the most common side effects since this is commonly tested.

Describe the best practices for performing a prostate biopsy.

1. Use transrectal ultrasound
2. Perform a prostatic block with local anesthesia
3. Try to avoid sending more than 2 specimens, whole, per container

The zones to sample were described in the conclusions of AUA/Optimal Techniques of Prostate Biopsy and Specimen Handling White Paper:

"In selecting locations for sampling, clinicians should use templates that incorporate adequate sampling of the apex or anterior apex; the far-lateral region, including the base, midgland, and apex; and the traditional sextant sites. Transition-zone sampling does not have a substantial impact on CDR [cancer detection rates], NPV [negative predictive value] or predictive ability. The use of a 12-core sampling strategy that incorporates apical and far-lateral cores appears to be optimal. …"

(https://www.auanet.org/common/pdf/education/clinical-guidance/Prostate-Biopsy-WhitePaper-Updated2015.pdf at p. 14)

He tolerates the prostate biopsy without incident—he was found to have a 65 gm prostate on ultrasound.

What is your next step?

Ask for the biopsy results.

Pathology from his prostate biopsy: 4 of 12 cores positive for Gleason 3+4 cancer, all with > 50% positivity from the R mid and base locations.

What is your assessment now?

65-year-old AAM with intermediate risk prostate cancer, clinical stage T1c.

Make sure you comment on what you believe his life expectancy is.

You determine that his life expectancy is > 10 years.

Make sure you know the clinical staging for prostate cancer.

Tx		primary tumor cannot be assessed
T0		no evidence of tumor
T1		tumor non-palpable nor visible by imaging
	T1a	tumor found incidentally in TURP specimen representing 5% or less of the resected tissue
	T1b	tumor found incidentally in TURP specimen representing greater than 5% of the resected tissue
	T1c	tumor identified by needle biopsy of the prostate (i.e., elevated PSA)
T2		tumor confined within the prostate
	T2a	tumor confined to less than one half of one lobe of the prostate
	T2b	tumor size is greater than one half of one lobe of the prostate, but not both lobes
	T2c	tumor involves both lobes of the prostate
T3		tumor palpable outside of the prostate
	T3a	extracapsular extension (unilateral or bilateral)
	T3b	tumor invades seminal vesicle(s)
T4		tumor is fixed or invades adjacent structures other than seminal vesicles: bladder, levator muscles, and/or pelvic wall

Republished with permission of Springer-Verlag New York Inc, from AJCC Cancer Staging Manual, Edge SB, 7th ed. ©2009; permission conveyed through Copyright Clearance Center, Inc.

Review the NCCN risk categories for prostate cancer.

Very low risk	must have all of the following: T1c, Gleason Score ≤ 6, PSA <10, Fewer than 3 prostate biopsy cores positive, ≤50% cancer in any core, PSA Density < 0.15 ng/mL/g
Low risk	T1-T2a, Gleason score ≤6, PSA < 10
Intermediate risk	T2b, T2c or Gleason 7 or PSA 10–20
High risk	T3a or Gleason 8–10 or PSA > 20
Very high risk	T3b, T4 or Primary Gleason 5, or > 4 Cores positive with Gleason 8–10

What are his risks of EPE and LN involvement?

MSKCC predicted pathologic features are:

Organ confined disease	41%
EPE	57%
LN involvement	3%
SV invasion	3%

Be prepared to discuss the different nomograms available for pre-operative assessment—MSKCC Nomogram, Partin Tables, Briganti Nomogram, etc.

What are the indications for pre-operative staging with imaging per the NCCN guidelines?

Bone Scan if any of the following T1 and PSA > 20; T2 and PSA > 10; Gleason Score ≥ 8; T3, T4; Symptoms concerning for metastases.

Pelvic CT or MRI if any of the following: T3, T4; T1-T2 and nomogram indicated probability of lymph node involvement > 10%.

Note: Prostate MRI is not listed as standard in the guidelines for the pre-operative work up for prostate cancer, but many surgeons use it for pre-operative planning for margins/nerve sparing. If you order an MRI, make sure you have justification for ordering it.

What are the basics of prostate MRI?

It should be a multiparametric (mp) exam performed with either a 1.5 Tesla magnet with an endorectal coil or a 3 Tesla magnet without an endorectal coil.

The parameters for the mpMRI should be a T2 weighted image, diffusion weighted imaging (DWI) and dynamic contrast enhanced imaging (DCE). Many centers also use an apparent diffusion coefficient (ADC) map to help further define the lesion seen.

T2	dark in the peripheral zone is concerning for cancer
DWI	bright in the corresponding T2 lesion is concerning
DCE	early enhancement with early washout of the corresponding T2 lesion is concerning
ADC	dark in the corresponding T2 lesion is concerning.

What are his treatment options?

Based on the NCCN guidelines:

1. Radical prostatectomy with pelvic lymph node dissection if his nodal risk is ≥2% (this patient fits this criteria)

2. External beam radiation therapy (EBRT) with 4–6 months of androgen deprivation therapy (ADT)
3. EBRT + brachytherapy with 4-6 months of ADT
4. Brachytherapy alone
5. Observation if life expectancy is < 10 years

What are the differences between radiation and surgery and the risks for both?

1. Surgery:

    Pros: PSA becomes an excellent tumor marker after surgery, there is a pathologic specimen which can help define risk category more precisely and accurately (30% upgrading at prostatectomy compared to biopsy), one-time treatment, can be performed minimally invasively.

    Cons: invasive, anesthetic required with antecedent risk, recovery required with time off work and limitation of activity level. Risks include death (<0.1%), hemorrhage (<5%), infection, positioning injury affecting the fibular and ulnar nerves, injury to rectum (1%), bladder/bladder neck contracture (<5%), obturator nerves and iliac vessels. Risk of positive margins (up to 20%) and needing adjuvant therapy with either radiation or ADT or both.

2. Radiation:

    Pros: non-invasive (except for brachytherapy), no real recovery, very low risk of infection/hemorrhage.

    Cons: higher risk of bowel/bladder dysfunction both acutely (50%) and long term (5%) (higher with brachy compared to EBRT), no pathologic specimen, PSA does not perform as well as a tumor marker, fatigue.

    Note: Both surgery and radiation seem to have similar rates of impotence (based on age and pre-operative function) and incontinence (5–10%), but these manifest earlier with surgery than with radiation.

He elects for a radical prostatectomy.

What is your pre-operative evaluation and how do you consent the patient?

Labs: Chem 7, CBC, Coags, Urine drug screen given his history of cocaine abuse
Tests: CXR, EKG (given his age and HTN and hypercholesterolemia)
Bowel Prep: can be omitted completely, enema is optional

During your pre-operative evaluation, make sure you discuss getting informed consent for the procedure, which includes all reasonable alternatives including observation, risks of the procedure and anesthesia, positioning injury and damage to surrounding structures (bladder, bladder neck contracture, rectum, obturator nerves, iliac vessels, etc.)

Make sure you also inform the patient about the risks of positive margins and the possible need for adjuvant therapy (ADT, EBRT, etc.) as well as the risks for impotence and incontinence.

Describe the AUA guidelines on DVT prophylaxis.

The AUA defines the following as increasing the risk for developing a DVT with surgery: Surgery, trauma (major or lower extremity); immobility/paresis; malignancy; cancer therapy; previous DVT; increasing age; pregnancy and the postpartum period; estrogen-containing oral contraception or hormone replacement therapy; acute medical illness; heart or respiratory failure; IBD; nephrotic syndrome; myeloproliferative disorders; obesity; smoking; varicose veins; central venous catheter, thrombophilia.

Based on the guidelines, patients should be placed into one of the following risk categories:

Low risk:	Minor surgery in patients <40 years with no additional risk factors
Moderate risk:	Minor surgery in patients with additional risk factors. Surgery in patients aged 40–60 years with no additional risk factors
High risk:	Surgery in patients > 60 years of age. Surgery in patients aged 40–60 with additional risk factors
Highest risk:	Surgery in patients with multiple risk factors

By Procedure

Transurethral surgery:

"For the vast majority of transurethral procedures, early ambulation is recommended for DVT prophylaxis. For patients at increased risk of DVT undergoing transurethral resection of the prostate (TURP), the use of GCS (graduated compression stockings), IPC (intermittent pneumatic compression devices), postoperative LDUH (low dose, unfractionated heparin) or LMWH (low molecular weight heparin) may be indicated."

"The prevention of DVT in patients undergoing anti-incontinence and pelvic reconstructive surgeries should be dictated by preoperative individual patient risk factors and procedure specific risk factors for DVT formation.

- For low-risk patients undergoing minor procedures the use of early postoperative ambulation appears to be sufficient.
- For moderate-risk patients undergoing higher risk procedures, the use of IPC, LDUH, or LMWH should be utilized.
- For high-risk and highest-risk patients undergoing higher-risk procedures, combination therapy with IPC plus LDUH or LMWH should be utilized unless the bleeding risk is considered unacceptably high."

Urologic laparoscopic and/or robotic assisted urologic laparoscopic procedures:

"[T]he Panel recommends the use of IPC devices at the time of the laparoscopic procedure. High-risk groups which may require the use of LDUH and LMWH may be identified."

Open Urologic Surgery:

"The Panel recommends the use of IPC in patients undergoing open urologic procedures. Given the increased risk factors within this patient population, in many patients undergoing open urologic procedures, more aggressive regimens combining the use of IPC with pharmacologic prophylaxis may be considered."

Conclusions of the AUA Guidelines:

"DVT prophylaxis should be considered in all patients undergoing urologic surgical procedures. In many patients undergoing low-risk procedures, early ambulation may be the only DVT prophylactic measure that is indicated. However, in patients with a high-risk profile undergoing a high-risk procedure, an assessment of all risk factors inherent to the patient and planned procedure should dictate the appropriate DVT prophylaxis."

Source: Forrest JB, Clemens JQ, Finamore P, et al. Best Practice Statement for the Prevention of Deep Vein Thrombosis in Patients Undergoing Urologic Surgery. J Urol 2009;181(3):1170–7. Copyright © 2009 by American Urological Association. Published by Elsevier Inc. Used with permission. (https://www.auanet.org/common/pdf/education/clinical-guidance/Deep-Vein-Thrombosis.pdf)

What is your approach?

Go with the approach you feel most comfortable with and be able to describe the key/critical steps. Make sure you mention pre-operative antibiotics, use of mechanical and chemical DVT prophylaxis. Also, make sure you comment on positioning and how you will take care to prevent positioning injury.

1. Robot assisted laparoscopic retropubic radical prostatectomy with pelvic lymph node dissection
    a. Robotic/Laparoscopic Key Steps:
        i. Position in lithotomy—describe protecting the fibular nerve
        ii. Supine—describe protecting the ulnar nerves when tucking the arms
2. Laparoscopic retropubic radical prostatectomy with pelvic lymph node dissection
    a. Laparoscopic/robotic Key Steps:
        i. Describe gaining access with either Veress or Hassan technique
        ii. Describe efforts at preventing injury during access: drop test, checking opening pressure with gas insufflation, using a visual obturator with camera insertion
3. Open retropubic radical prostatectomy with pelvic lymph node dissection

All procedures, discuss the following standard steps:

1. Entering the space of Retzius
2. Isolating and ligating the dorsal venous complex
3. Separating the bladder and prostate
4. Athermal dissection of the seminal vesicles and vas deferens
5. Blunt and athermal dissection of the posterior plane between the rectum and prostate
6. Antegrade or retrograde nerve sparing procedure
7. Preservation of urethral length
8. Vesico-urethral anastomosis
9. Pelvic lymph node dissection

What are your boundaries for a pelvic lymph node dissection on this patient?

Note: If performing a pelvic lymph node dissection, opt for an extended template as this identifies metastatic disease twice as often as a standard lymph node sampling.

The boundaries are: all nodal tissue around the external iliac vein anteriorly, the pelvic side wall laterally, the bladder wall medially, the floor of the pelvis posteriorly, Cooper's ligament distally, and the internal iliac artery proximally. Many urologists will also include the external iliac artery and common iliac artery in an extended template.

You and your patient elect for a robot assisted laparoscopic radical prostatectomy.

During insufflation, the patient becomes severely bradycardic with a heart rate of 12 and hypotensive.

What is your differential diagnosis?

1. Cardiac event
2. Air Embolus
3. Vagal response to pneumoperitoneum

What do you do?

1. Look into the abdomen if a port has been placed to inspect for injury
2. Desufflate the abdomen to release the intra-abdominal pressure
3. Listen to the lungs for cogwheel murmur indicating an air embolus

You rapidly desufflate the abdomen and the patient's HR recovers. Anesthesia tells you that he is stable and that you can continue the operation.

What do you do?

1. You can convert to open, if you feel more comfortable with this approach
2. You can reinsufflate the abdomen at a lower flow rate which exerts pressure less quickly on the patient

You select to reinsufflate and the patient insufflates without difficulty. Anesthesia gives you a thumbs up to continue the operation. The procedure goes well, including a bilateral nerve sparing procedure, up to the point where you have to transect the dorsal venous complex. In doing so, the complex slips out of the stitch and the patient begins to bleed significantly from the open venous sinuses.

What do you do?

1. Instruct your assistant to suction judiciously to preserve your pneumoperitoneum
2. Turn the pneumoperitoneum pressure up to 20mmHg, if the patient can tolerate it
3. If you are unable, you can tightly pack a sponge/raytec/lap into this area to buy time so that you can get the necessary equipment ready to deal with the bleeding

After turning the pressure up to 20 and packing the DVC, you are able to insert needle drivers and another suture and completely ligate the DVC.

You then complete the procedure as planned. After completing the anastomosis, you extract the specimen and test the anastomosis, for which there is no evidence of leak. You elect to leave a drain in place and awake the patient and transfer him to the recovery room.

Be prepared to discuss other potential intra-operative complications.

1. Rectal injury
    a. If a sharp injury and less than 1.5 cm in size, it is safe to close primarily
        i. Leave a pelvic drain and advance the diet slowly
    b. If the patient has been radiated (salvage prostatectomy), strongly consider diversion with a colostomy and consult a colorectal or general surgeon to do this
        i. If surgeon unavailable, be prepared to discuss how to create an end colostomy/ileostomy
    c. If it is a thermal injury, make sure to debride the edges prior to closing
    d. Depending on the size, you may consider an end colostomy
2. Nerve transection
    a. Be prepared to discuss intra-operative repair of the obturator nerve
    b. It is ok to ask for a neurosurgical consult. However, they will likely be unavailable
    c. You would repair the nerve with the assist of the robotic magnification or loupes or the microscope, depending on your level of comfort
    d. You should close the perineural tissue in one layer with interrupted 6-0 non-absorbable, monofilament sutures and ensure that the nerve is tension free after repair
3. Secondary hole (button hole) of the bladder
    a. This most often happens when dissecting the posterior bladder neck off of the prostate. If you identify this intra-operatively, you should be prepared to repair it
    b. Make sure to inspect the bladder neck for potential damage to the ureteral orifices and when repairing the hole, and you may want to insert 5 Fr catheters in the ureters to help identify them and avoid injury
    c. Leave a pelvic drain and discuss the need for a cystogram prior to catheter removal

    Note: Leaving a pelvic drain has become controversial. There is mounting evidence that it can be omitted after a non-complicated prostatectomy, so be prepared to defend your answer, regardless of which you pick.

The patient recovers well and is transferred to the floor. About 6 hours later, you receive a call from the nurse that the patient is in severe pain and that his urine output has decreased significantly over this time.

What do you do?

Make sure you mention that you will come in and examine the patient.

What information will you want?

Vitals	T38.6C	HR: 120	RR: 20	BP 170/95
General	looks to be in pain			
Heart	tachycardic, regular			
Lungs	clear B, tachypneic			
Abdomen	soft, distended with pain to palpation in his pelvis. His JP has a large amount of serosanguinous fluid in it			

GU	significant ecchymosis around his penis and scrotum, Foley catheter with minimal urine in the drainage tubing
Ext	no edema

What is your differential diagnosis?

1. Cardiac event
2. PE
3. Hemorrhage
4. Unrecognized bowel injury
5. Clogged Foley catheter

What do you do next?

Send labs:

CBC
BMP
Troponins/CKMB
EKG—sinus tachycardia
JP for creatinine level

Would you like to do anything while you wait for the labs to return?

You hand irrigate the Foley catheter and you are able to extract an obstructing clot. The bag immediately fills with 500 mL of urine and the patient's pain resolves. His JP output decreases significantly and he thanks you.

The remainder of his labs return normal and you remove his JP drain prior to him being discharged home the next day with his Foley catheter.

What next?

Say that you will see the patient back to remove his Foley/Staples and to review his pathology.

His pathology shows pT2c, N0, Mx, margins negative, Gleason 3+4 in 25% of the gland.

What is your next step?

1. You should recommend Kegel exercises to help recover his continence
2. You can offer early penile rehabilitation with a PDE5I, although the evidence for this is conflicting. Also, this could be expensive, and your patient may not be able to afford it
3. You should arrange for a repeat PSA in about 1 month

He sees you back in 1 month and says his incontinence is down to 1 pad per day and that he still has not tried to have erections. His PSA is undetectable.

What are his options for his lack of erections at this point?

1. Observation—1 month is likely too soon for him to see an improvement in erections

2. A PDE5I—be prepared to discuss the side effects of the medication you choose (blue-green visual changes for Viagra, muscle aches for Cialis, flushing and nasal congestion for all and the remote risk of priapism for all)
3. Intracavernosal injections (Trimix, Alprostadil, etc.)—again, be prepared to discuss the side effects of these medications (i.e., risk of priapism, pain at injection site, development of penile curvature from scarring)
4. Vacuum Erection Device—discuss the pros and cons of this (successful, but "floppy erections," possible ecchymosis if not using a pressure regulated device, pain with the constriction band)
5. Penile prosthesis—last resort

Your patient elects for observation and at his 6-month visit, says he is having erections with penetrative intercourse. His PSA remains undetectable. He and his wife thank you.

CASE 2

HPI: 39-year-old male self refers to you because his brother in law (55-years-old) was recently diagnosed with prostate cancer. He is a healthy male with no lower urinary tract symptoms (IPSS 3) and good erections SHIM (25).

PMH: HTN

Allergies: none **Medications:** Metoprolol

SH: left knee arthroscopy; (-) tob; (-) ETOL; no use illicit drugs
FH: brother-in-law with prostate cancer; patient does not know the PSA or Gleason score at diagnosis; he believes that his brother-in-law has treated it with radiation therapy; no first-degree relatives with prostate cancer
ROS: negative for 12 systems reviewed

What would you do next?

Mention that you would examine the patient from head to toe starting with the vitals.

PE:

Vitals	T 38.6	BP: 103/70	RR: 8	BMI 23
GA	healthy, young male; NAD			
HEENT	WNL			
Heart	bradycardic; regular			
Lungs	unlabored; clear bilaterally			
GU	penis circumcised, normal; scrotum and testes, normal			
DRE	do not offer this patient a DRE			
Ext	no edema			

After examining the patient and reassuring him that there are no findings to suggest prostate cancer, he demands to have a PSA drawn.

What do you do?

You should review the updated AUA guidelines on early detection of prostate cancer.

The guideline statements:

"1. The Panel recommends against PSA screening for men under 40 years. In this age group, there is a low prevalence of clinically detectable prostate cancer, no evidence demonstrating benefit of screening and likely the same harms as other age groups.
2. The Panel does not recommend routine screening in men between the ages of 40 to 54 years at average risk. For men under 55 years at higher risk (positive family history or African American Race), decisions regarding prostate cancer screening should be individualized.
3. For men aged 55 to 69 years of age, the Panel recognizes that the decision to undergo PSA screening involves weighing the benefits of preventing prostate cancer mortality in one man for 1000 men screened over a decade against the known potential harms associated with screening and treatment. For this reason, the Panel strongly

recommends shared decision making for men aged 55–69 years of age who are considering PSA screening and proceed based on a man's values and preferences.

4. To reduce the harms of screening, a routine screening interval of two years or more may be preferred over annual screening in those men who have participated in shared decision making and decided on screening. As compared to annual screening, it is expected that screening intervals of two years preserve the majority of the benefits and reduce over-diagnosis and false positives. Additionally, intervals for rescreening can be individualized by a baseline PSA level.
5. The Panel does not recommend routine PSA screening in men age 70+ years or any man with less than a 10 to 15-year life expectancy. Some men age 70+ years who are in excellent health may benefit from prostate cancer screening."

Source: Carter HB, Albertsen PC, Barry MJ, et al. Early detection of prostate cancer: AUA Guideline. J Urol. 2013 Aug;190(2):419–26. doi: 10.1016/j.juro.2013.04.119. Epub 2013 May 6. Copyright © 2013 American Urological Association. Published by Elsevier Inc. Used with permission.
https://www.auanet.org/common/pdf/education/clinical-guidance/Prostate-Cancer-Detection.pdf

He thanks you for the information but wants to know what the benefits and harms of screening are.

Benefits:

With aggressive screening, we have seen a stage migration of detected cancers to lower stages and grades at diagnosis. There has been a reduction in the number of men who present with metastatic disease by almost 75% in the United States. ERSPC (European screening trial) showed a reduction of men presenting with metastatic disease of about 30% in the screened arm when compared to the control arm.

The decrease in prostate cancer mortality since the advent of PSA screening has not been established as causal, but instead associative. As a result, it is controversial to claim that PSA screening has led to decreased prostate cancer mortality.

Harms:

Elevated PSAs usually lead to prostate biopsies. The harms of prostate biopsy include: hematuria (14–50%), hematochezia, hematospermia (10–70%), dysuria, and retention, pain and infection. The 30-day risk of hospitalization is estimated at 4%, of which 75% are due to infectious complications.

Over-diagnosis of indolent prostate cancer is a harm of biopsy as most of these men typically initiate treatment without the definitive benefit of cancer specific or overall survival. Finally, psychological stress can occur as a result of prostate cancer screening from negative biopsies, unnecessary biopsies to the diagnosis of indolent disease.

You explain all of this to your patient and he thanks you for sitting with him and taking the time to review the pros and cons of prostate cancer screening. He agrees with you that screening does not seem like such a good idea anymore.

CASE 3

HPI: 76-year-old Caucasian male with significant lower urinary tract symptoms and back pain. His symptoms are mainly hesitancy and some feelings of incomplete emptying. His IPSS is 15 and his SHIM is 15.

PMH: HTN, Afib, DMII

PSH: (-) tob, former smoker, quit > 20 years ago; (-) ETOH; no illicit drugs

Allergies: none **Medications:** Lisinopril, Xarelto, Insulin

SH: ex-lap many years ago from a gunshot wound with a bowel resection
FH: father with prostate cancer, brother with prostate cancer; does not know the grade, stage or treatment status of either
ROS: negative except for his sharp back pain that he says is constant but worse at the end of the day

What next?

Make sure you ask about his performance status and how you elicit this information from your patients. He is ECOG 0 and relatively healthy and spry.

PE:

Vitals	T 38.8 C BP 155/90 RR 12 BMI 33
General	NAD; looks stated age
HEENT	WNL
Heart	RRR; no MRG
Lungs	unlabored; clear bilaterally
Abdomen	soft; large midline scar from sternum to pubic symphysis; no evidence of masses
GU	penis uncircumcised, glans, meatus normal; testicles and scrotum normal bilaterally
DRE	good rectal tone; prostate is about 60 g, he has a large nodule on the left lobe that is firm; it feels confined to the prostate and takes up more than half of that lobe; borders of the prostate are easily palpated
Ext	no edema
Spine	has pain with palpation over his lower back that reproduces the pain he mentioned to you earlier

What initial lab tests do you order?

UA → WNL
UCx → no growth
CBC → WNL
BMP → WNL
PSA → 7.8

What is age adjusted PSA and what are the traditional values used in this manner to determining a "normal"?

Age	PSA
40–49	0–2.5 ng/mL
50–59	0–3.5ng/mL
60–69	0–4.5 ng/mL
70–79	0–6.5ng/mL

Adapted from Harvard Health newsletter: http://www.health.harvard.edu/newsletter_article/PSA-Prostate-Specific-Antigen-Persisting-Scientific-Ambiguities

What next?

You should offer the patient a prostate biopsy based on his PSA and DRE findings.

You can offer the patient a prostate MRI with fusion guided biopsy based on his DRE findings.

Your patient's insurance does not cover his MRI and he elects for a prostate biopsy.

How do you prepare him for his prostate biopsy?

See CASE 1.

Make sure that he is off all blood thinners prior to the biopsy.

Make sure that you give the patient informed consent prior to his procedure which should include a discussion of the alternatives to the procedure as well as the risks/benefits of the procedure.

Describe your procedure for a prostate biopsy

See CASE 1.

You prescribe you patient 500 mg ciprofloxacin as a one-time dose prior to the procedure. You perform a prostate biopsy without incident.

The patient calls you the next morning complaining of perineal pain and some chills. It is your clinic day so you tell him to come in and see you.

What do you do?

Examine the patient from head to toe starting with the vitals.

Vitals	T: 104	HR: 120	BP: 75/44	RR: 30
General	looks ill; somnolent			
HEENT	WNL			
Heart	tachycardic; irregular rhythm			
Lungs	labored breathing; decreased breath sounds bilaterally			
Abdomen	soft; non-tender; non-distended			
GU	penis, scrotum, testicles normal			
DRE	gentle DRE reveals a boggy prostate with pain on palpation			

What is your assessment?

Post-biopsy sepsis.

What do you do next?

You arrange for the patient to go to the ED to be stabilized and recommend to them that they send a urine culture, blood cultures and place a Foley catheter.

The ER physician calls you and says that your patient looks "sick." He is febrile and having chills and rigors. He recommends admission to the ICU for peri-operative antibiotics. He had a difficult time in placing the Foley, so you came to the ED and placed the Foley yourself. Your patient is admitted.

That night, the nurse calls you from the ICU stating your patient is experiencing extreme penile pain and swelling that cannot be resolved with IV narcotics.

What do you do?

Go see the patient and examine him.

His vitals are stable. His exam is concerning for a swollen glands penis that is exposed. His Foley catheter is in place and draining clear yellow urine.

What is your diagnosis and why did it occur?

Paraphimosis, you forgot to place the foreskin back to anatomic position after placing the Foley catheter. You reduce the paraphimosis and your patient thanks you.

What next?

Ask for the urine and blood cultures.

The blood and urine cultures return with E. coli resistant to Ciprofloxacin. You start him on culture specific antibiotics based on his culture results.

Your patient stabilizes after 2 days of IV antibiotics and is discharged home on day 3 with 2 weeks of culture specific antibiotics.

How could you have prevented his prostate biopsy related infection?

You could have sent a pre-biopsy peri-rectal swab culture for Ciprofloxacin resistant organisms or treated him based on the antibiogram for the region in which he lives. This should be available from your hospital's infection control department or your infectious disease doctor.

What next?

Ask for the pathology.

His pathology reveals Gleason 3+4 disease in 6 of 12 cores, located at the left base and mid.

What is this patient's stage and risk score?

Stage T2b and intermediate risk based on the NCCN guidelines (see CASE 1).

Does he need any imaging for staging?

Yes, he has lower back pain and therefore warrants a bone scan.
His bone scan is negative for metastases.

What are his treatment options?

Based on the NCCN guidelines, his treatment options are:

1. Radical prostatectomy with PLND
2. EBRT with 4–6 months ADT
3. EBRT with Brachytherapy with 4–6 months ADT
4. Brachytherapy

What are some potential downsides to performing a prostatectomy on this patient?

1. Advanced age
2. Previous intra-abdominal and pelvic surgery from GSW
    a. This could increase his risk of collateral damage during access and the procedure for prostatectomy
3. Post-biopsy prostatitis/sepsis which can impact tissue planes at prostatectomy

After reviewing both radiation and surgery with him in detail (see CASE 1), he wishes to be referred to a radiation oncologist and start external beam radiation therapy. He completes radiation therapy and 6 months of ADT and his PSA nadirs at 0.2 off of all ADT. He returns to your clinic 24 months later with a PSA that is 12.3 after having been lost to follow up.

Describe the definitions for PSA recurrence following radiation therapy.

ASTRO: 3 consecutive rises of PSA from the nadir
Phoenix: Nadir + 2

Based on this definition, he has had a biochemical recurrence, what is your next step?

State that you will take a thorough history and physical.

History: He has had increasing back pain that is new for him and weight loss. He has some lower urinary tract symptoms, but these are minimally bothersome.

Physical exam: He has pain over his lower back that is severe. He has mild weakness of his lower extremities. On DRE, his rectal tone is slightly decreased and you can palpate a mass on his prostate.

What is your assessment?

Metastatic prostate cancer with possible cauda equina syndrome.

What is your next step?

You have him emergently admitted to the hospital and consult neurosurgery who confirms spinal cord compression due to bony metastasis with an MRI and treats him appropriately. The rest of his metastatic work up is negative.

What is the next step?

Androgen deprivation for metastatic prostate cancer.

What are the options for androgen deprivation?

Be prepared to discuss the mechanism of action and potential side effects for all of these medications.

General side effects form androgen deprivation:

1. Body habitus changes—gynecomastia, testicular atrophy, loss of muscle mass, increase in fat
2. Elevation of lipids and cholesterol
3. Diabetes
4. Cardiovascular disease—controversial, but likely
5. Anemia
6. Fatigue—very common
7. Osteoporosis
8. Sexual dysfunction—decreased libido, ED
9. Infertility
10. Hot Flashes—common

Commonly used androgen deprivation:

1. Non-steroidal Anti-Androgens—work by inhibiting the androgen receptor. Side effects include gastrointestinal upset and liver toxicity with the risk for gynecomastia
2. Androgen Synthesis inhibitors:
   a. Ketoconazole with Prednisone—works by inhibiting multiple cytochrome p450 enzymes. Also inhibits production of glucocorticoids and mineralocorticoids. Castrate by 8 hours
   b. Abiraterone—selective inhibitor for CYP 17. Increased aldosterone. May see electrolyte abnormalities as a side effect
   c. LHRH Agonists—stimulate LHRH receptors in the pituitary and lead to an initial surge in LH and FSH and a subsequent flare in testosterone. Continued LHRH agonist leads to suppressed testosterone, usually after 30 days
3. GnRH Antagonists—block GnRH receptors in the pituitary. These do not cause a flare. Makes men castrate within days. Can cause an increase in LFTs

This patient should be offered medication for bone health given his metastatic disease. Calcium and vitamin D—controversial.

AUA Guideline on castrate resistant prostate cancer (CRPC):

> "[I]t is impossible to make firm recommendations regarding the use of supplemental calcium and vitamin D in prostate cancer patients who will experience bone mineral density loss from long-term ADT. Practitioners who choose to recommend these supplements should be aware of the potential risks and benefits."

Based on the AUA guidelines, you should also start the patient on medications for bone health:

> "Clinicians may choose either denosumab or zoledronic acid when selecting a preventative treatment for skeletal related events for mCRPC patients with bony metastases."

Source: Cookson MS, Roth BJ, Dahm P, et al. Castration-resistant prostate cancer: AUA guideline. J Urol. 2013;190(2):429–38. Copyright © 2013 American Urological Association. Published by Elsevier Inc. Used with permission. https://www.auanet.org/common/pdf/education/clinical-guidance/Castration-Resistant-Prostate-Cancer-PG.pdf

You start the patient on ADT and Denosumab with supplemental Ca.

What is your follow up?

You obtain a PSA 1 month later and it is 0.1 and remains this value for another year. At that time, his PSA returns to 2.5.

What is your next step?

You check a serum testosterone and it is at castrate levels (<30ng/dL).

What is your assessment?

He now has CRPC.

What is your next step?

You should perform a thorough history and physical.

You should ask questions related to symptoms from his CRPC to help categorize him into one of the 6 index patients presented in the AUA guideline on CRPC cited above.

1. Asymptomatic non-metastatic CRPC
2. Asymptomatic or minimally-symptomatic, metastatic (m) CRPC without prior Docetaxel chemotherapy
3. Symptomatic, mCRPC with good performance status and no prior Docetaxel chemotherapy
4. Symptomatic, mCRPC with poor performance status and no prior Docetaxel chemotherapy
5. Symptomatic, mCRPC with good performance status and prior Docetaxel chemotherapy
6. Symptomatic, mCRPC with poor performance status and prior Docetaxel chemotherapy

Your patient states that he feels well and has recovered his lower extremity strength and is voiding well with normal BMs. His back pain has resolved and his weight is stable.

What is your next step?

You restage him and all of his staging studies come back negative for metastases.

What is your next step?

Based on the AUA Guidelines, he represents index patient 1. The preferred management strategy for this patient is continued observation with repeat PSAs and continued ADT. Make sure you know the AUA guidelines for CRPC.

What is your follow up?

You continue to follow his PSA, and over the next 2 years he has other medical conditions that worsen. He has suffered a mild stroke and has had an MI with resultant CHF. His ECOG performance status is ECOG 3. His PSA has continued to rise and is now 45. His repeat imaging reveals widespread metastatic disease and he has pain from these.

What are your options?

Based on the AUA Guidelines, his poor performance status excludes him from Docetaxel-based chemotherapy. He should be offered a multidisciplinary palliative care treatment plan which should focus on supporting his physical, psychosocial, spiritual and social symptoms.

Your patient passes away a few months later and you receive a letter from his wife thanking you for helping him find peace at the end of his life.

Case 4

HPI: 59-year-old male with PSA of 4.5. He is otherwise healthy and has minimal LUTS with an IPSS of 4 and a SHIM of 24.

PMH: HTN

PSH: (-) tob; (-) ETOH; no illicit drugs

Allergies: PCN **Medications:** none

FH: no prostate cancer
SH: appendectomy at 22 years of age; left hip replacement about 3 years ago.
ROS: negative × 12 systems reviewed.

What would you do next?

PE:

Vitals	T 102 BP 155/87 RR 12 BMI 35
General	comfortable
HEENT	AT/NC
Heart	RRR; no MRG
Lungs	unlabored; clear bilaterally
Abdomen	soft; non-tender; non-distended; no masses
GU	penis is circumcised; scrotum and testicles normal
DRE	normal rectal tone; prostate is smooth, symmetric and 40 g
Ext	no edema

What is your next step?

UA → normal

What is your assessment?

59-year-old healthy M with an elevated PSA.

What options does the patient have?

1. Observation with a repeat PSA
2. Prostate biopsy
3. Prostate MRI with fusion biopsy (see Cases 1 and 3)

Your patient is very nervous and elects for a prostate biopsy.

Perform a rectal culture and treat the patient based on this result with the appropriate antibiotic(s). Make sure that he is off all blood thinners prior to the biopsy.

Make sure that you give the patient informed consent prior to his procedure which should include a discussion of the alternatives to the procedure as well as the risks/benefits of the procedure.

What are the AUA recommendations for antibiotic prophylaxis in patients with a previous joint replacement?

Antimicrobial prophylaxis is not indicated for urologic patients on the basis of orthopedic pins, plates, and screws, nor is it routinely indicated for most urologic patients with total joint replacements on that basis alone.

Antimicrobial prophylaxis intended to reduce the risk of hematogenous total joint infection is recommended in patients who meet BOTH sets of criteria listed below:

1. Increased risk of hematogenous total joint infection
    a. Patients during the first two years after prosthetic joint replacement
    b. Immunocompromised patients with a prosthetic joint replacement: inflammatory arthropathies, drug induced immunosuppression, radiation induced immunosuppression
    c. Patients with prosthetic joint replacements and comorbidities: previous prosthetic joint infections, malnourishment, hemophilia, HIV infection, diabetes, malignancy
2. Increased risk of bacteremia associated with urologic procedures
    a. Any stone manipulation
    b. Any procedure with transmural incision into the urinary tract
    c. Any endoscopic procedure of the upper tract
    d. Any procedure that includes bowel segments
    e. Transrectal prostate biopsy
    f. Any procedure with entry into the urinary tract in individuals with higher risk of bacterial colonization: indwelling catheter or intermittent cath, indwelling ureteral stent, urinary retention, history of recent/recurrent UTIs; urinary diversion.

The recommended antimicrobial regimen in these patients include:

1. A single systemic level dose of a Quinolone (e.g., Ciprofloxacin, 500 mg; Levofloxacin, 500 mg; Ofloxacin, 400 mg) orally 1 to 2 hours preoperatively.
2. Ampicillin 2 gm IV (or Vancomycin 1 g IV over one to 2 hours in patients allergic to Ampicillin) plus Gentamicin 1.5 mg/kg IV 30 to 60 minutes preoperatively.
3. For some procedures, additional or alternative agents may be considered for prophylaxis against specific organisms and/or other infections.

For patients NOT meeting BOTH of these criteria, antimicrobial prophylaxis still may be indicated to reduce the risk of other infections.

Adapted from: Antibiotic prophylaxis for urological patients with total joint replacements. J Urol 2003;169(5):1796–7. Copyright © 2003 American Urological Association. Published by Elsevier Inc. Used with permission.

Describe your procedure for a prostate biopsy.

See CASE 1.

The patient's rectal swab reveals Cipro resistant E. coli that is sensitive to Cefazolin, Nitrofurantoin, and Trimethoprim-Sulfamethoxazole.

You decide to give him both Ciprofloxacin and TMP-SMX.

What is the mechanism for TMP-SMX and the side effects of the medication?

TMP/SMX works by inhibiting the metabolism of folate in bacterial cells and causes cell death. Side effects include nausea, vomiting, rash, and diarrhea as well as severe allergic reactions (Stevens-Johnson syndrome) and C. diff diarrhea.

He undergoes a prostate biopsy without incident and calls you 3 days later asking about the pathology report. His pathology reveals 2 cores of Gleason 6 disease with <10% in both cores, 1 from the right base and 1 from the left base. You call him into the clinic to discuss his results.

What is his clinical stage and risk group?

T1c—Very low risk (see CASE 1).

What are his disease management options based on the NCCN guidelines?

If his life expectancy is > 20 years the options are: Active Surveillance, EBRT or brachytherapy or RP with PLND if >2% risk of nodal metastases.

If his life expectancy is 10–20 years, the preferred strategy is Active Surveillance.

If his life expectancy is < 10 years, observation is the preferred management strategy.

What is active surveillance (AS)?

AS is expectant monitoring of very low risk prostate cancer in a man with > 20 year life expectancy. Treatment for cure should commence when disease progression has occurred (increase in disease volume, increase in Gleason grade, etc.)

What are the benefits and risks/disadvantages of AS?

Benefits:	No treatment means no side effects. You can eliminate a majority of over-treatment and associated side effects with AS.
Risks:	Very low, but real risk of missing the opportunity to cure the patient at the time of diagnosis. Periodic prostate biopsies may be necessary which carry an antecedent risk.

After lengthy discussion, the patient elects for AS.

How will you confirm that his disease fits the entry criteria for AS?

You can perform another biopsy of the prostate (if you select this and your patient becomes septic, see CASE 2) His final path confirms very low risk disease.

You can offer an MRI; however, his hip replacement results in a poor image quality and he, therefore, requires a repeat biopsy, see above.

Finally, you confirm that the patient has very low risk disease and that he is appropriate for AS.

What is your follow up protocol?

PSA no more often than every 6 months unless clinically indicated.
DRE no more often than every 12 months unless clinically indicated.
Repeat prostate biopsy no more often than every 12 months unless clinically indicated.

How many men will avoid any treatment because of AS?

67%

Your patient enters into your prescribed AS protocol and is thrilled that he can continue to live life as usual.

Recommended Reading/Bibliography (all can be found via internet search):

NCCN Guidelines for prostate cancer
AUA Best Practice Policy Statement on Urologic Surgery Antimicrobial Prophylaxis
AUA Best Practice Statement on Prevention of Deep Vein Thrombosis in Patients Undergoing Urologic Surgery
AUA White Paper on Optimal Techniques of Prostate Biopsy and Specimen Handling
AUA Best Practice Statement on PSA Testing for the Pre-Treatment Staging and Post-Treatment Management of Prostate Cancer
AUA White Paper on the Quality Improvement Summit 2014: Conference Proceedings on Infectious Complications of Transrectal Prostate Needle Biopsy
Castration-Resistant Prostate Cancer: AUA Guideline

CHAPTER 6

RENAL CELL CARCINOMA

EDWARD RAMPERSAUD, MD

CASE 1

HPI: 48-year-old Caucasian male evaluated by his primary care provider for vague, intermittent upper abdominal pain. The pain was not associated with weight loss, nausea, vomiting, or timing of PO intake. His PCP ordered an abdominal ultrasound that revealed a 3 cm right lower pole renal mass.

PMH: (+) HTN

PSH: left inguinal hernia repair

Allergies: none **Medications:** Captopril

FH: non-contributory
SH: (+) tob, 30 pack year; (+) ETOH, social
ROS: non-contributory

PE:

Vitals	T 98.3	BP 160/60	P 68	RR 10
GA	middle-aged CM INAD			
HEENT	benign			
Heart	RRR			
Lungs	CTA			
Abdomen	soft; NT/ND; (-) masses			
Flank	benign			
GU	normal phallus; testicles, epididymis and vasa WNL			
Rectal	benign; (-) masses			
Ext	(-) CCE			
Neuro	non-focal			

What initial lab tests do you order?

UA → WNL
CBC → WNL
Chem 7 → Cr 1.2 mg/dL
LFTs → WNL

What is your initial work-up?

State that you would obtain a dedicated CT scan of the abdomen and pelvis with and without contrast to evaluate the renal mass. You also need a CXR for staging purposes.

CT abd/pelvis: 3 cm exophytic, heterogeneous enhancing mass (that enhances from 35 HU to 80 HU) located in the right lower pole; the right kidney is otherwise normal; the left kidney is normal
Prompt bilateral excretion and no hydronephrosis
No lymphadenopathy, no evidence of metastasis

CXR: normal

What is your assessment?

48-year-old, overall healthy CM with an enhancing right-sided small (< 4 cm) renal mass.

What additional studies does this patient need?

None.

1. A chest CT is indicated if the CXR is abnormal
2. An MRI is indicated if the CT scan suggests renal vein invasion or adrenal pathology not fully characterized by the CT scan
3. Bone scan is warranted if new-onset bone-type pain or alk phos is elevated
4. Brain imaging is reserved for patients with advanced disease or according to corresponding symptoms

Is this likely to be benign or malignant?

Based on size, and age/gender of patient, there is an 85–90% likelihood of this being a malignant lesion.

Should the mass be biopsied?

Probably not.

1. If biopsied and deemed malignant, it will be treated
2. If biopsied and deemed benign, such as an oncocytoma, there is still reason to treat against potential for mass-effect
3. The only conceivable rationale for biopsy in this setting would be regarding either active surveillance or thermoablative treatment

What are the treatment options at this time?

1. Active surveillance
2. Percutaneous thermoablation (cryo/RFA)
3. Partial nephrectomy
4. Radical nephrectomy

What is your recommendation?

All recommendations, if given at all, should be based upon the expected advantage gained when all the patient factors, tumor factors, and intervention factors are taken into consideration.

In a patient this young with relatively minimal comorbidity, and good performance status, a primary recommendation per the AUA Guidelines would be partial versus radical nephrectomy.

Most experts agree that nephron-sparing surgery (NSS) should be the standard of care. Radical nephrectomy, however, is an acceptable alternative when NSS would be to the detriment of the patient or would be technically unfeasible (such as a very central/hilar tumor with a normal contralateral kidney).

In this case, with a polar SRM, partial nephrectomy is rather straightforward to the well-trained urologist. As such, this should likely be the primary recommendation.

That being said, the role for active surveillance in this setting is unknown. Additionally, through large retrospective data analysis, thermoablation may have an equivalent effect. Partial/radical nephrectomy, however, require much less-intense follow-up imaging.

At the end of the day, there are several possible "correct" answers; and a cogent and detailed conversation is required to discern what would best suit the patient.

The patient decides to have you perform a partial nephrectomy.

Whether the circumstances are best suited for a robotic or open partial, describe the major differences between the 2 exposures and potential sequelae of the operation.

1. Location
    a. There is no "location" best suited for robotic versus open partial nephrectomy
    b. It has more to do with the surgeon's comfort, which is often reason enough to perform one over the other
    c. Some might consider anterior, lateral, or lower pole locations somewhat easier to expose
2. Discuss with the patient (usually at the clinic visit):
    a. The increased risk of hemorrhage or urine leak when performing partial nephrectomy as opposed to a radical nephrectomy
    b. The possible need for completion nephrectomy in the circumstances of uncontrolled hemorrhage or positive frozen surgical margins beyond which no more margin is available
    c. Review the objectives, benefits, associated risks, and likely recovery course of surgical treatment
    d. Obtain informed consent
    e. Perform a pre-operative evaluation, including pre-operative labs, T&C blood, and EKG, and order IV antibiotics
    f. Prior to surgery, confirm the side of surgery and ensure that films are available intraoperatively

Discuss your surgical technique.

The Operation (Extraperitoneal Flank Approach–for example)

1. Positioning
    a. Following induction of anesthesia, place a Foley catheter to monitor urine output during the perioperative period
    b. Place and activate sequential compression stockings
    c. Position the patient in the left lateral decubitus position (left side down) with the table in flexion to increase the space between ribs
        i. All pressure points should be padded adequately
        ii. Patient should be secured to the surgical table and the right arm should be supported in an anatomic position to prevent a brachial plexus injury
2. Incision
    a. Incise the skin between the 11th and 12th rib and dissect through the flank muscle layers, taking care to avoid or minimize dissection through perforating nerves
    b. Enter the retroperitoneum by dividing the lumbodorsal fascia, taking care to avoid entry to the right pleura posteriorly and peritoneum anteriorly
3. Exposure and mobilization

   a. Mobilize the right kidney within Gerota's fascia posteriorly, laterally, superiorly and anteriorly
   b. Identify the ureter to prevent inadvertent injury
   c. Once adequately mobilized, place the kidney on anterior and medial traction to assist with identification and isolation of the renal vessels
   d. Dissect and isolate the right renal artery posteriorly with care for possible later temporary occlusion
   e. Identify the right renal vein anteriorly
   f. De-fat the kidney in the area of the renal mass with care to maintain a fat pedicle that can be used for reconstruction if needed
   g. Use intra-operative ultrasound if necessary to define the boundaries and depth of the mass and assist with planning of the resection

4. Resection and reconstruction
   a. Administer 12.5 g mannitol and intravenous fluids
   b. Clamp the renal artery or use a parenchymal clamp if appropriate
   c. Place an isolating pad around the kidney and surround the kidney with ice slush (when artery clamped)
   d. Incise the renal capsule 1 cm away from the tumor edge
   e. Excise the mass with a negative surgical margin
   f. Sample areas of the tumor bed if there is concern regarding incomplete excision
   g. Assess for collecting system entry and repair if present
   h. Achieve hemostasis with focal suture ligatures, electrocautery and hemostatic agents/products
   i. Reconstruct and reinforce the defect with absorbable bolsters
   j. Remove the vascular clamp as soon as possible
   k. Assess for arterial pulse and perfusion of the kidney
   l. Assess for adequacy of hemostasis
   m. Re-approximate the perinephric fat pedicle over the reconstruction if necessary
5. Closure
   a. Place and secure a percutaneous drain in proximity to the right kidney—if deemed necessary
   b. Inspect the retroperitoneum, peritoneal boundary and pleura
   c. Inspect the renal vasculature for good flow—palpable pulse/thrill and soft vein
   d. Inspect the kidney for return of good turgor and color
   e. Remove the flexion from the surgical table and re-approximate the ribs if necessary
   f. Close the muscle and fascial layers
   g. Close the skin

Does this patient need an adrenalectomy?

No. In patients with small lower pole tumors and normal CT findings of the adrenal, an adrenalectomy is not necessary given the very low risk of involvement.

What if the tumor were in the upper pole?

Not unless the tumor is contiguously involving the adrenal. If the adrenal is without its own mass, and the tumor is not directly involving the adrenal, the ipsilateral adrenal is at a statistically similar risk of developing a met as the contralateral adrenal. As such, the ipsilateral adrenal should remain in situ if radiographically and physically within normal limits.

Discuss potential intra-operative complications.

1. Potential sources of venous bleeding
    a. Inferior vena cava/gonadal vein avulsion from cava
        i. Obtain proximal and distal control with sponge sticks
        ii. Oversew the injury with 5.0 Prolene
    b. Lumbar vein retracts into the psoas muscle
        i. Oversew the muscle with deep bites of figure of 8
    c. Adrenal vein avulsion
        i. Control the bleeding with Allis clamp
        ii. Oversew the injury
2. Injury to duodenum during Kocher maneuver
    a. Oversew the laceration in 2 layers
    b. Keep NPO and use NGT to decompress stomach post-operatively until bowel function returns
3. Injury to liver during retraction
    a. Direct pressure and Surgicel or Avitene or argon coagulator
    b. Oversew the injury with figure of 8
4. Pleural entry
    a. Repair the pleural defect
    b. Use a catheter or red rubber tube to suction the chest and reduce the pneumothorax
    c. Complete the repair and closure under suction to reduce the chances of a retained pneumothorax
    d. Place a temporary chest tube if the pleural defect is too large to repair or the pneumothorax cannot be reduced
    e. Obtain a CXR in the recovery room
5. Ureteral injury
    a. Identify site of injury
    b. Debride devitalized tissue if necessary
    c. If possible, repair primarily
    d. Place stent in setting of substantial repair, such as following dismemberment or large repair

Your patient did well from his surgery and was transferred to the recovery room.

What is your post-operative care?

1. Monitor post-operative renal function with serum creatinine determinations
2. Monitor post-operative blood counts
3. Encourage aggressive ambulation
4. Await return of bowel function

On post-operative day 3, your patient develops significantly increased drainage from his flank drain.

How do you proceed with evaluation?

Send the drain fluid for a creatinine determination.

The drain creatinine returns 21.0. His serum creatinine is 1.1.

What is the diagnosis?

Urine leak.

How would you proceed?

1. The vast majority of urine leaks close with conservative management
2. Small leaks can be managed conservatively with observation or manipulation of the drain to ensure that the drain is not actively contributing to the leak
3. Large or persistent leaks may require urinary diversion with an indwelling ureteral stent until the leak is resolved
    a. However, the stent placement may exacerbate the leak, requiring indwelling Foley catheterization to prevent vesicoureteral reflux
4. Secondary closure, fistula repair or nephrectomy are rarely required in challenged cases of nephrocutaneous fistula

You adjust the drain and ensure it is not on active suction. Over several days, the drainage decreases significantly. You re-check the fluid for a creatinine determination and find it is 1.2, and then remove the drain. He recovers uneventfully.

Discuss the algorithm for managing renal fistula after partial nephrectomy:

Algorithm for Managing Renal Fistula

Leak from drain site
↓
Take off suction
↓
Adjust drain away from anastomosis
↓
Insert retrograde stent
↓
Place nephrostomy tube
+
Percutaneous drainage of urinoma
↓
Insert antegrade stent

Almost all urine leaks will heal/scar closed over time with conservative management and maximal drainage. It may require several months of serial exams and clinic visit, however.

What is your follow-up?

Ask for the pathology report.

Pathology report:	Renal cell carcinoma (clear cell type) with negative margins; Fuhrman grade 2, tumor was confined within the renal capsule but was located within 2 mm of the surgical margin

What is his pathologic stage?

Stage I (pT1aNxMx).

What are the most important prognostic determinants in renal cell carcinoma?

1. Local tumor extent and tumor size (stage)
2. Histologic subtype
3. Surgical margin status
4. Regional nodal metastasis
5. Evidence of distant metastatic spread
6. Performance status

What is the importance of the tumor within 2 mm of the surgical margin?

Although the tumor came in close proximity of the surgical margin, several studies have demonstrated that a distance of < 1 cm to a negative margin is not associated with higher rates of local recurrence.

What would the significance be of a positive margin?

There would a slightly higher risk of local recurrence, but with adequate surveillance, there would be no statistically higher risk of disease-specific mortality. If a recurrence/persistence is noted, consideration could be given to all modalities as previously described.

How are you going to follow this patient?

This patient is at low risk for locally recurrent disease/metastatic progression.
It may be best to subscribe to a Guideline recommendation such as the NCCN Guidelines.

A reasonable first step would be to obtain new baseline imaging 3–6 months after surgery to affirm good perfusion/function of the preserved kidney.

Discuss the staging system for RCC:

Renal Cell Carcinoma (TNM Stage Classification):

Tx	Cancer stage unknown
To	No evidence of cancer
T1	≤ 7 cm; confined to kidney
T1a	≤ 4 cm; confined to kidney
T1b	> 4 cm but ≤ 7 cm; confined to kidney
T2a	> 7 cm but < 10cm; confined to kidney
T2b	> 10cm but confined to kidney
T3	Confined to Gerota's fascia
T3a	Tumor directly involves the perirenal or sinus fat, or is growing into the renal vein; but not beyond Gerota's fascia
T3b	Tumor grossly extends into the vena cava below the diaphragm
T3c	Tumor grossly extends into vena cava above diaphragm or the wall of the vena cava
T4	Involvement beyond Gerota's fascia or direct involvement of the adrenal gland
Nx	Nodal involvement unknown
No	No evidence of nodal involvement

N1	Regional nodal involvement
Mx	Distant metastasis unknown
Mo	No evidence of distant metastasis
M1	Distant nodal or organ metastasis present

Republished with permission of Springer-Verlag New York Inc, from AJCC Cancer Staging Manual, Edge SB, 7th ed. ©2009; permission conveyed through Copyright Clearance Center, Inc.

What are some risk factors for RCC?

1. Family history
2. Smoking (cigarettes, cigars, pipes)
3. Hereditary RCC syndromes
4. Obesity
5. Dialysis

Note: About 2% of RCC are associated with inherited syndromes.

What is the pathogenesis of clear cell RCC?

1. Arises from proximal convoluted tubule
2. Associated with defects of the VHL gene (60% of sporadic RCC)

How is the association of defects in the VHL gene and the development of clear cell RCC explained?

VHL protein, the product of the VHL gene, functions as a tumor suppressor by inducing ubiquitination of hypoxia-inducible factor (HIF). When the VHL protein is mutated, HIF is not degraded, and this yields the transcription of pro-growth genes. In the absence of a normal VHL protein, HIF accumulation results in downstream growth factor production such as VEGF, GLUT-1, TGF-α, PDGF, etc.

Is RCC a single pathological entity?

No. Over the last 25 years much groundbreaking work in science at large has been made through advances in the genetic, molecular, and metabolic understanding of RCC.

Though under the RCC umbrella, the many different histological subtypes are genetically, phenotypically, and pathologically distinct. More subtypes are identified with increasing frequency.

CASE 2

HPI: 43-year-old Caucasian male presents with left flank pain and a single episode of gross hematuria to his PMD who calls you. You ask him to send the patient right over to your office with only the physical exam and lab work below. You see him and he denies any nausea, vomiting, diarrhea, unintentional weight loss, early satiety or any constitutional symptoms.

PMH: none

PSH: tonsillectomy

Allergies: none **Medications:** none

FH: non-contributory
SH: (+) tob, 20 pack year ; (+) ETOH; (-) IVDU; occupation, athletic trainer
ROS: non-contributory

PE:

Vitals	T 98.6	BP 120/60	P 63	RR 12
GA	middle-aged CM INAD			
HEENT	benign			
Heart	RRR			
Lungs	CTA			
Abdomen	soft; NT/ND; not HSM, normoactive bowel sounds, (-) masses			
Flank	(-) CVAT			
Pelvic	unremarkable			
Rectal	normal tone; BCR intact			
Ext	(-) CCE; good pedal pulses			
Neuro	non-focal			
Lymph nodes	(-) adenopathy			

What initial lab tests do you order?

UA → 10–15 RBC/HPF; (-) WBC, 0–5 bacteria
Chem 7 → Cr 1.1 mg/dL
CBC → WNL
Cytology → (-) malignant cells
Culture → no growth

What is your initial work-up?

State that you would get a CT to evaluate the upper tracts and arrange for an office cystoscopy.

Cystoscopy: negative for abnormal lesions, no stones

CT scan: 7.5 cm enhancing left renal mass (centrally located)
The right kidney appears normal; both adrenal glands are seen and are clearly separate from the mass; normal liver; renal vein and vena cava are normal; retroperitoneal lymph nodes are not enlarged

What is your assessment?

43-year-old CM with a central left renal mass.

What are some of your concerns regarding central renal masses?

1. Most commonly, central lesions will still be conventional RCC
2. However, a major consideration should be given to the possibility that this is a primary urothelial lesion
3. Depending on various patient-related factors, consideration needs to be given to the possibility of medullary RCC (SC trait), collecting duct carcinoma, and metastatic lesion

What do you do now?

Need to do metastatic work-up. Obtain CXR. Obtain liver function tests with alkaline phosphatase. If alk phos is elevated or if patient is complaining of bone pain, a bone scan is indicated.

CXR:	Normal
LFTs:	WNL
Alk phos:	WNL

What can you do to help narrow down your treatment options?

You could consider urine cytology and diagnostic ureteroscopy.

This could be important because if the patient is suffering from an upper tract urothelial carcinoma (UTUC), then consideration should be given to neoadjuvant chemotherapy with the affected kidney in situ prior to nephroureterectomy.

You perform a urine cytology and ureteroscopy. They are both negative.

What is your recommendation?

Laparoscopic (transperitoneal vs RP) or open nephrectomy.

Describe your operative technique:

The Operation (Transperitoneal Laparoscopic Nephrectomy)

1. After intubation, ensure that a Foley catheter is in place and an NG tube is placed
2. Position the patient in the right lateral decubitus position (usual 45° angle) and pad all pressure points to prevent nerve compression injury (peroneal nerve, brachial plexus stretch injury)
3. Determine trocar placement to triangulate to kidney
4. Obtain access to begin insufflation—describe both Hasson and Veress techniques
    a. Veress technique
        i. Make incision at location of first trocar site (camera, umbilical site)
        ii. Use Kelly clamp to spread away underlying fat and identify fascia
        iii. Grasp the fascia using a Kocher clamp and place 2 stay sutures into the fascia

        iv. While applying upward traction to the sutures, pass the Veress needle gently feeling 2 pops to enter abdomen
        v. Using a 10 cc syringe, inject 5 cc saline without force to confirm intra-peritoneal position
        vi. Advance the needle about 1 cm, and there should be no resistance
            aa. It is crucial to hold the needle steady during these maneuvers since radial motion of the needle could exacerbate any injury if one is present
        vii. Confirm a low starting intra-abdominal pressure
        viii. Remove the Veress needle and then place initial trocar through this site, attach gas to trocar and pass camera to visually inspect abdominal contents to confirm clean entry
    b. Hasson technique
        i. Considered a safe method of access for patients with previous abdominal surgery
        ii. The initial steps are the same as above; however, after identifying the fascia, it is incised and then the peritoneum is incised
        iii. Once this is done, 2 heavy sutures are placed on either side of the incision to incorporate the fascia and peritoneum, and the Hasson trocar is put in place and insufflation started

5. Place working trocars under direct vision
6. Take down colon along the white line of Toldt, with care taken to not enter Gerota's fascia. Splenic flexure is mobilized to allow the colon to drop out of the surgical field
7. Care must be taken to not injure the tail of the pancreas
8. Ureter is identified on the psoas
9. Gonadal vein is identified and traced to the renal hilum
10. The renal vein is skeletonized, with care taken to not avulse the insertion of the adrenal vein or the lumbar vein, which is often seen entering on the posterior aspect of the renal vein (questions that can be asked here include collateral drainage of the adrenal gland, L kidney, or L testicle)
11. The renal artery is then identified posterior and superior to the renal vein. If a renal artery inferior or anterior to the renal vein is found, then it is not the primary renal artery
12. Secure the renal artery with either Weck Hem-o-lock clips or endo GIA stapler. If clips are used, 2–3 clips are placed proximally and 1 distal (kidney side)
13. Take the vein with an endo GIA stapler
14. Proceed to take the gonadal vein and ureter, and finally dissect free the posterior, lateral, and superior aspects of the kidney and place in a laparoscopic bag
15. Extraction techniques vary, but key point is to ensure that the kidney is placed in a laparoscopic bag to facilitate removal with minimal risk of incision site implants
16. Port sites should be closed if they are >10 mm in diameter

What are potential intraoperative complications and management?

1. Positioning injuries
    a. Ensure that all pressure points are well padded
        i. Brachial plexus
        ii. Lateral popliteal nerve
        iii. Femoral nerve
        iv. Sciatic nerve

    b. Common mild palsies will resolve in 4–6 weeks, but severe forms may last up to 2 years
2. Insufflation/access related complications
    a. Gas embolism
        i. 0.002 to 0.02% with mortality of 50%
        ii. “Millwheel” cardiac murmur, cardiovascular collapse after insufflation, head and neck cyanosis, dysrhythmias, hypoxia, decreased end-tidal CO2
        iii. Treatment
            aa. Terminate insufflation
            bb. Release pneumoperitoneum
            cc. Left lateral decubitus positioning (right side up)
            dd. Cardiopulmonary resuscitation
            ee. Aspiration of gas via central line
            ff. Oxygenation with 100% O2
    b. Veress needle or trocar placement injury
        i. Incidence 0.03–0.3%
            aa. If there is a strong suspicion of major vascular injury, needle should be left in place and access obtained by a second Veress needle placement or Hasson technique to identify the location of injury. Veress needle injury can often be repaired laparoscopically with intracorporeal suturing
            bb. If trocar injury is suspected, open conversion, exploration and repair are the tenets to follow. Do not remove the trocar until conversion is made to best identify the location and severity of the injury
    c. Extraperitoneal insufflation
        i. Suspected with high initial intra-abdominal pressures after small volume is insufflated
        ii. Subcutaneous emphysema, pneumoscrotum, pneumothorax, pneumomediastinum
        iii. Treatment—reposition insufflation needle
3. Vascular complications
    a. Risk of vascular injury is 2–3%
    b. Management based on severity of injury
        i. Clip vessel if it can be easily identified and can be clipped without repercussions
        ii. Transient increase of intra-abdominal pressure to slow venous ooze
        iii. Apply pressure with rolled cotton gauze or instrument
        iv. Biosealants may be helpful for persistent venous ooze or parenchymal surface ooze
        v. Oversew vessel laparoscopically if amenable
        vi. Convert to open or hand assist procedure if any concerns, leave an instrument on the vessel/bleeding area to ensure easy identification once conversion is done
    c. Lower pressure to 5 mm Hg at end of case to ensure that there is no active bleeding and watch trocar removal to verify no abdominal wall bleeding
    d. Post-operative signs of delayed hemorrhage
        i. Prolonged pain, abdominal distention, tachycardia and fall in hematocrit
            aa. CT abd/pelvis to look for hematoma
            bb. Treatment: observation to re-exploration dependent on severity of symptoms
4. Hollow viscus complications
    a. Incidence of 0.13–0.8 %
        i. 50% of all injuries due to electrocautery
        ii. 30% during access—needle/trocar
        iii. 20% “blind” passage of instruments

- b. 69% were not recognized at the time of surgery
  - i. For those recognized intraoperatively, consideration of laparoscopic repair. Key to have copious antibiotic irrigation and placement of aerobic and anaerobic antibiotic coverage
  - ii. Signs of bowel injury in the post-op patient
    - aa. Trocar site pain
    - bb. Fever
    - cc. Leucopenia with a left shift
  - iii. Low threshold for CT imaging with oral contrast and delayed views to ensure contrast is in the descending colon
- c. 80% of injuries treated with laparotomy

5. Solid viscus complications
   - a. Liver/spleen
     - i. Often occur during placement of Veress needle, primary trocar, or during retraction
       - aa. Evaluate for organomegaly on preoperative imaging and place primary trocar/Veress needle away from organ
       - bb. Gentle retraction
     - ii. Minor injuries can be treated laparoscopically
       - aa. Biosealants
       - bb. Argon beam (ensure that you vent the abdomen since pressures increase with argon gas)
       - cc. Cellulose gauze
     - iii. Open repair if above methods fail
   - b. Kidney trocar injury
     - i. If Gerota's is intact, there is a stable retroperitoneal hematoma, and the patient is hemodynamically stable, conservative observation may be carried out
     - ii. Explore kidney if:
       - aa. Expanding hematoma
       - bb. Vascular instability
       - cc. Unknown extent of injury

What is the role of lymphadenectomy during radical nephrectomy?

1. Currently, evidence supporting lymphadenectomy in kidney cancer is incomplete and there are no standard recommendations
2. In general, lymph node dissections are not routinely performed in stage I or stage II disease, particularly when a partial nephrectomy is used to remove the tumor
3. Prognostication from nodal staging may be helpful for future strategizing of care. There *may* be a possible therapeutic benefit, although this remains unproven

The patient is discharged home on POD #2 but calls the office on POD #6 complaining of abdominal pain and subjective fevers.

What do you do?

See the patient in the office, obtain a detailed history, and perform a physical examination.

History reveals that the pain is most severe around the umbilical trocar site, and there is nausea, vomiting, and no appetite.

Physical findings reveal a temp of 102°. Examination does not reveal erythema around the trocar site or a palpable hernia; however, his abdomen is rigid.

What is your impression and plan?

The patient likely has a bowel injury, or possibly a strangulation near the port-site. Have the patient admitted for NG decompression, hydration, fever work-up, IV antibiotics, and observation while awaiting results of a CBC and CT of the abdomen and pelvis with contrast.

CBC results: $WBC = 1.8 \times 10^9$
$HCT = 41$

You obtain a CT of the abdomen and pelvis with oral contrast.

Results reveal the presence of free air in the abdomen and free contrast adjacent to the descending colon.

What is your assessment?

Bowel injury likely to the descending colon.

What do you do now?

1. Exploratory laparotomy with general surgery consultation for evaluation and repair of the bowel injury
2. If the peritoneum is relatively clean, a primary anastomosis with a generous margin to account for thermal injury to bowel can be performed, followed by copious antibiotic irrigation
3. If the abdomen has copious stool, then a diverting colostomy with a Hartman's procedure would be recommended; however, this should be performed with the assistance of a general surgeon

You performed an exploratory laparotomy with general surgery and identified a descending colon perforation. A primary repair was performed, and the patient subsequently recovered without further event.

What is your follow-up?

Ask for the pathology results.

Pathology report: renal cell carcinoma (clear cell type) with negative margins; the tumor is confined to the renal capsule and measures 7.2 cm in diameter

What is his pathologic stage?

pT2NxMx or stage II renal cell carcinoma.

CASE 3

HPI: 69-year-old Caucasian female who presents with abdominal pain. She denies gross hematuria or other types of pain; positive for weight loss, fatigue, and abdominal pain. She does not report any constitutional symptoms such as fevers or chills; + 30 pack year smoking

PMH: (+) HTN

PSH: hysterectomy
(B) oophorectomy

Allergies: none **Medications:** Captopril

FH: non-contributory
SH: (+) tob, 30 pack year; (+) ETOH
ROS: positive for weight loss, fatigue, and abdominal pain
ROS: non-contributory

PE:

Vitals	T 98.6	BP 160/90	P 90	RR 12
GA	WF INAD			
HEENT	benign			
Heart	RRR			
Lungs	CTA			
Abdomen	soft; NT/ND; (+) fullness of her left abdomen			
Flank	(-) CVAT			
Pelvic	WNL			
Rectal	normal tone; BCR intact			
Ext	(-) CCE; good pedal pulses			
Neuro	non-focal			
Lymph nodes	(-) adenopathy			

What initial lab tests do you order?

UA → 10–15 RBC/HPF; (-) WBC
Chem 7 → Cr 1.42 mg/dL
CBC → WNL

What is your initial work up?

State that you would obtain a CT scan of the abdomen and pelvis with delayed images, given her symptoms and hematuria. Recommend a cystoscopy to complete the hematuria evaluation.

Abdominal CT scan:	7 cm upper pole, solid, exophytic, enhancing left renal mass; (R) kidney appears small; both adrenal glands are seen; (L) adrenal gland appears separate from the renal mass; normal liver; retroperitoneal lymph nodes are not enlarged; inferior vena cava appears normal
Cystoscopy:	normal

What is your assessment?

69-year-old CF with a large left renal mass and a small right kidney.

What is your differential diagnosis?

Differential diagnosis includes primary renal tumor, urothelial tumor of the kidney, or metastatic tumor. Less likely to be a primary sarcoma or lymphoma.

What is your impression?

She most likely has RCC of the left kidney.

What do you do now?

Need to do metastatic work-up. Obtain CXR, liver function tests with alkaline phosphatase. If alk phos is elevated or if patient is complaining of bone pain, obtain bone scan.

CXR: WNL
LFTs: WNL
Alk phos: WNL

What is your assessment now?

Stage II (T2NxMx) renal tumor.

How would you proceed?

Given the atrophic right kidney, a reasonable argument could be made to perform a Lasix renal scan (or differential nuclear scan of your choosing) to determine how much of a global renal impact is made by the right kidney.

Another take on the situation is to assume that the right kidney does not have much contribution to the global renal function based on its appearance and as such, recommend complex partial nephrectomy as a primary option.

You recommend a renal scan which reveals split function of 70% left and 30% right.

What is your recommendation?

Left partial nephrectomy.

State that you would obtain an informed consent by discussing the surgical procedure, indications, potential risks, and complications. Obtain pre-operative laboratory tests and anesthesiology evaluation. Consult thoracic surgery for management of the solitary pulmonary lesion.

Labs: Chem 7, CBC, PT, PTT, platelets
Tests: CXR, EKG
Blood: T&C for 2 units PRBCs
SCDs
IV antibiotics

She agrees to surgery and gives consent.

What is your surgical approach?

Be prepared to discuss your surgical approach and the operative technique.

Surgical incision may include:

1. Anterior subcostal (chevron)
2. Flank (between10th and 11th rib)
3. Midline

Describe your operative technique:

The Operation (Partial Nephrectomy)

1. Extraperitoneal flank incision
2. Incise over 11th or 12th rib
3. Open Gerota's fascia and free up the entire kidney
4. Leave the perirenal fat over the tumor and dissect out hilar vessels
5. Place a vessel loop around the renal artery and vein separately
6. Cool the kidney with ice slush (if warm ischemia time > 30 minutes)
7. Place a vascular bulldog on the renal artery or entire hilum if required
    a. May include Mannitol 12.5 g
8. Incise the capsule 2 cm away from the tumor margin
9. Send frozen-section of the margins and the tumor itself
10. Suture ligate arcuate vessels with 4-0 chromic sutures (figure of 8 fashion)
11. Close kidney upon itself or cover the defect with hemostatic materials
    a. Hemostatic materials:
        i. Perirenal fat
        ii. Omentum
        iii. Peritoneal graft
        iv. Gelfoam
        v. Any and all other hemostatic agents you like
12. Release the bulldog clamp
13. Place a drain and close the incision

What do you do if collecting system has been violated?

1. Suture ligate interlobar vessels, including adjacent infundibulum
2. Place internal stent
3. Close the collecting system in watertight fashion with 4-0 absorbable suture
4. Reinforce the repair and close as described above

Do you need to remove the left adrenal gland?

No.

What is your follow-up?

Ask for the pathology results.

Pathology report: renal cell carcinoma (clear cell type) with negative margins. The tumor is confined to the renal capsule and measures 7.2 cm in diameter

What is her pathologic stage?

pT1bNxMx or stage I.

On POD #2, she develops left flank pain and her drain expresses blood discharge.

What is your impression and plan?

Obtain a detailed history and perform a physical examination. Obtain a STAT CBC. She most likely has developed a discrete bleed from her resection bed.

You send a CBC.

Hemoglobin = 8.5 mg/dL
Hematocrit = 26.0 mg/dL

Immediately following surgery, her HCT was 32.

What is your assessment?

Post-surgical hemorrhage.

What do you do now?

1. Make sure she is hemodynamically stable. Administer IV fluids, transfuse with blood if necessary. Consider transfer to a monitoring setting if needed
2. Consider involving Interventional Radiology to perform angiography/embolization (especially if continuing to bleed)
3. If she stabilizes, conservative therapy may be all that is needed
4. If her hematocrit continues to fall despite conservative and supportive management, selective angioembolization may be required
5. If she is unstable, urgent angioinfarction or surgical exploration and nephrectomy may be necessary

She was hemodynamically stable and did not require urgent observation or transfusion. A repeat CBC later in the day showed continued decrease in HCT to 22. You transfused her 2 units of PRBC and obtained an abdominal CT scan. The CT scan revealed a left retroperitoneal hematoma.

You contacted IR to request angiography and possible angioembolization. Left renal angiography revealed a discrete single source of bleeding from a branch of the apical segmental artery that was selectively embolized successfully.

Her HCT stabilized and she recovered without incident.

What is the preferred management of tumors in solitary kidney or bilateral simultaneous tumors?

1. Solitary kidney
    a. In-vivo partial nephrectomy with local hypothermia
    b. Ex-vivo bench surgery with autotransplantation
    c. Radical nephrectomy with dialysis and delayed transplantation
2. Bilateral kidney tumors
    a. Radial nephrectomy and partial nephrectomy
    b. Bilateral partial nephrectomy
    c. Bilateral radical nephrectomy with dialysis and delayed transplantation

What are the indications for partial nephrectomy?

1. Bilateral RCC
2. Solitary kidney with RCC
3. Patient with bilateral renal disease who will progress to renal failure if radical nephrectomy is performed
4. Indeterminate polar mass
5. Exophytic peripheral mass that is very small
6. Multiple small tumors

Describe the renal arterial anatomy:

1. Main renal artery
   a. Divides into anterior and posterior branches
   b. Divides into 4 or 5 segmental arteries
2. Branch
   a. First (posterior) branch supplies posterior segment of the kidney
   b. Second (anterior) branch supplies anterior segment of the kidney
   c. Four anterior segmental arteries: apical, upper, middle, lower anterior
3. Segmental artery
   a. Enter the renal sinus to give off lobar arteries
4. Lobar artery
   a. Lobar arteries divide and enter the parenchyma as interlobar arteries
5. Interlobar artery
   a. Courses next to column of Bertin
   b. It parallels infundibuli and calyces
   c. Stops at corticomedullary junction and gives off arcuate artery
6. Arcuate artery
   a. Runs parallel to the corticomedullary junction
   b. Gives off interlobular artery
7. Interlobular artery
   a. Feeds the afferent arterioles of glomeruli

What are the complications of partial nephrectomy?

1. Intraoperative hemorrhage
2. Delayed bleeding
3. Persistent urine leak from collecting system
4. Perirenal abscess
5. Urinoma
6. Reno-cutaneous fistula
7. Acute tubular necrosis
8. Conversion to radical nephrectomy

What are the survival rate and the incidence of local recurrence after partial nephrectomy?

1. Survival rate is similar to that of radical nephrectomy
2. Risk of developing a tumor in contralateral kidney: 1–2%
3. Local recurrence rate for tumors <3 cm: <5%

CASE 4

HPI: 71-year-old Caucasian male presents with total painless gross hematuria. He has been experiencing intermittent hematuria for several weeks. This was not associated with urinary tract infection. He is currently not bleeding and has lost 20 lbs in the last 4 months without dieting. + low back pain. Has 40 pack year history of smoking, quit 4 years ago.

PMH: HTN
glaucoma

PSH: LIH repair

Allergies: none **Medications:** HCTZ, Betoptic eye drops

FH: non-contributory
SH: (+) tob, 40 pack-year; (+) ETOH
ROS: weight loss, abdominal pain, gross hematuria

PE:

Vitals	T 98.6	BP 140/60	P 90	RR 12
GA	elderly CM INAD			
HEENT	benign			
Heart	RRR			
Lungs	CTA			
Abdomen	soft; NT/ND; (-) masses; well healed left inguinal scar			
Flank	(-) CVAT			
GU	normal phallus; adequate meatus (B) testicles WNL			
Rectal	prostate @30 g smooth and benign; (-) nodularity guaiac (-); normal sphincter tone; intact BCR			
Ext	(-) CCE			
Neuro	non-focal			
Lymph nodes	(-) adenopathy			

Labs

UA → 5–10 RBC/HPF; (-) WBC
Chem 7 → Cr 1.2 mg/dL
CBC → WNL
Cytology → (-) malignant cells
PSA → 1.77 ng/mL

What is your initial work-up?

Hematuria evaluation.

CT abd/pelvis: 12 cm solid mass (R) upper pole of the kidney that enhances; normal liver; renal vein and vena cava normal; retroperitoneal

	lymph nodes are enlarged; (L) kidney is small; both adrenals are normal
Cystoscopy:	normal; both ureteral orifices effluxing clear urine

What is your assessment?

71-year-old CM with large (R) upper pole renal mass and small contralateral kidney.

What is your next step?

Need to perform metastatic work-up. Obtain CXR and liver function tests with alk phos. If alk phos is elevated or if patient is complaining of bone pain, need to obtain bone scan. May also decide to assess differential renal function since left kidney is small.

CXR:	multiple tumors (1 cm) studded throughout the lungs
LFTs:	elevated
Alk phos:	elevated
DMSA scan:	80% function on (R) and 20% function on (L)
Bone scan:	normal

What do you recommend at this point?

You could consider biopsy of the lung lesions, but in all likelihood, with the large renal mass and adenopathy, the lesions in the lung are overwhelmingly likely to be mRCC.

What is his clinical stage?

Clinical stage IV renal tumor.

What are his treatment options?

1. Observation
    a. No treatment is always an option that should be mentioned. However, in the examination setting, your examiner may make him experience recurrent hematuria, become hypotensive, and necessitate multiple blood transfusions
    b. At this point you need to discuss surgical options
2. Angioinfarction for palliative purposes
    a. The tumor may be infarcted using embolization technique with the idea of improving local control/preventing local complications such as bleeding
    b. If you follow this protocol, you must be prepared to perform laparotomy and take out the kidney if he develops complications from angioinfarction
    c. Risks of angioinfarction include post-infarction syndrome and systemic embolization (e.g., colon infarction)
3. Nephrectomy
    a. Nephrectomy (simple or radical) may be indicated for local control, i.e., prevention of recurrent bleeding or poorly controlled pain
4. Cytoreductive nephrectomy
    a. 2 well-designed trials have reported a survival advantage of patients with metastatic renal cell carcinoma that underwent nephrectomy prior to systemic

   immunotherapy compared to those patients that did not. The benefit was small, about 3 months
   b. Based on these studies, patients with good performance status and acceptable operative risk are offered nephrectomy prior to systemic immunotherapy as part of a multidisciplinary approach

5. Interferon therapy
   a. Interferons are a family of secreted proteins that induces antiviral, anti-proliferative, and immunomodulatory activities
6. Interferon α has been shown to cause regression of metastatic renal cell carcinoma. Complete and partial clinical responses occurred in < 1% and 15–20%, respectively IL-2 therapy
   a. IL-2 is 15 kilodalton glycoprotein produced by helper T cells. IL-2 produces lymphokine-activated killer (LAK) cells, enhances natural killer (NK) cell function, and mediates regression of metastatic cancer
   b. When high-dose IL-2 was used alone, 11% reported complete response and 8% reported partial response
   c. Despite its relatively low response rates, high-dose IL-2 therapy is currently still considered the gold standard for treating metastatic RCC, although several promising new agents are rapidly becoming available
7. New agents
   a. Multiple new oral agents have recently been FDA-approved for the treatment of metastatic RCC:
      i. VEGF blockade—Bevacizumab
      ii. VEGF inhibition—Sunitinib, Sorafenib, Pazopanib, Axitinib, Lenvatinib
      iii. mTOR inhibition—Temsirolimus, Everolimus
      iv. PD-1 inhibition—Nivolumab

   Note: Despite the availability of such new agents, the prognosis of patients remains poor. Strong consideration should be given to referring such patients to tertiary care centers and/or enrollment in well-designed clinical trials investigating new treatment options.

The patient underwent radical nephrectomy with subsequent immunotherapy.

What are indications for pre-operative arterial embolization?

1. Very select patients with large or locally invasive tumors
2. Difficult nephrectomy for a large tumor where significant blood loss is anticipated
3. Allows ligation of renal vein before renal artery

What are some complications of pre-operative arterial embolization?

1. Distal embolization
2. Flank pain
3. Fever
4. Malaise

What are the side effects of IL-2?

1. Fever, chills, malaise, nausea, vomiting, diarrhea
2. Pre-renal azotemia, hypotension, fluid retention, respiratory distress syndrome

Note: The mechanism for IL-2-induced multi-organ dysfunction is capillary leak syndrome, mediated by local production of nitric oxide by cells of the monocyte-macrophage lineage.

Is routine regional lymphadenectomy necessary?

1. Routine regional lymphadenectomy is not necessary
   a. Tumor spreads via blood and lymph with equal frequency
   b. Lymphatic drainage of kidney variable
   c. Patients without metastasis to lymph nodes can also develop disseminated metastasis
2. Aggressive surgery for patients with gross nodal involvement or multiple distant metastasis is unwarranted since it contributes little to survival

How do you manage bilateral renal cell carcinoma?

1. Bilateral partial nephrectomy in-vivo
2. Radical nephrectomy and partial nephrectomy
3. Ex-vivo excision and autotransplantation
4. Bilateral radical nephrectomy with dialysis

Note: Obtain renal function tests preoperatively. Operate on the kidney with less function first. If both kidneys have equal function, operate on the kidney that is more diseased.

CASE 5

HPI: 67-year-old Caucasian male with abdominal pain and distention for the past 6 months. He has lost his appetite and does not eat that much anymore. He has lost 15 lbs in the last 3 months. No other constitutional symptoms. No voiding problems. No hematuria.

PMH: none

PSH: none

Allergies: none **Medications:** none

FH: (-) prostate cancer
SH: (-) tob; (-) ETOH; retired
ROS: non-contributory

PE:

Vitals	T 98.6	BP 160/80	P 90	RR 12
GA	WDWN CM INAD			
HEENT	bilateral temporal wasting o/w benign			
Heart	RRR			
Lungs	CTA			
Abdomen	soft; distended; (+) fluid wave; tender RUQ; caput medusae (engorged anterior abdominal wall veins)			
Flank	(-) CVAT			
GU	normal circumcised phallus; adequate meatus; (B) testicles WNL; (R) varicocele → grade III			
Prostate	smooth and benign @ 20 g			
Ext	(-) CCE			
Neuro	non-focal			

What initial lab tests do you order?

UA	→	15 RBCs/HPF	
CBC	→	Hgb 9 g/dL	
Chem 7	→	WNL	
Alk phos	→	560 U/L	(28–120 U/L)
LFTs	→	Elevated AST/ALT	
PSA	→	1.4 ng/mL	(< 4.0 ng/mL)
PT/PTT	→	normal	

What would you do next?

State that you would obtain CT scan and urine cytology followed by cystoscopy.

CT scan (C+/C-):	15 cm (R) upper pole renal mass with renal vein thrombus; IVC with questionable thrombus; (-) lymphadenopathy; normal (L) kidney; abdominal ascites; dilated anterior abdominal wall veins
Cytology:	(-) malignant cells

Cystoscopy: benign appearing urothelium; both ureteral orifices with clear efflux of urine

What is your assessment?

67-year-old CM with large right renal mass with renal vein and possible caval thrombus.

What is his clinical stage?

Clinical stage III (T3bNxMx) RCC.

What is your next step?

State that you would obtain MRI, CXR, and bone scan. MRI is needed to better evaluate the vena caval thrombus. The elevated alk phos and/or bone pain requires you to obtain bone scan. CXR or chest CT scan is needed for additional staging.

CXR:	negative
Bone scan:	(-) for metastases
MRI:	caval thrombus above the hepatic vein (level III). No intrahepatic liver lesions suspicious for visceral metastases

Note: If MRI is contraindicated (e.g., metal hardware in body), may obtain trans-esophageal echocardiogram or IVC-gram with SVC-gram (rarely performed today).

What is your recommendation?

This patient needs radical nephrectomy with removal of vena caval thrombus.

State that you would obtain an informed consent by discussing the surgical procedure, indications, potential risks and complications.

Remark that you would obtain preoperative labs and tests. In addition, you would bowel prep this patient and place sequential compressive devices (SCD).

Given the level of the caval thrombus and evidence of hepatic obstruction, consider employing cardiothoracic assistance for on-pump veno-venous bypass. Circulatory arrest is rarely indicated, even for level IV thrombi.

Labs:	Chem 7, CBC, PT, PTT, platelets
Tests:	CXR, EKG
Blood:	T&C for 2 units PRBCs
Bowel prep:	mechanical prep
SCDs	
IV antibiotics	

He agrees to surgery and gives consent.

What is your surgical approach?

Be prepared to discuss your surgical approach and the operative technique.

Preferred approaches include chevron or thoracoabdominal (bed of 9th or 10th rib)

Describe your operative technique:

The Operation (Radical Nephrectomy via thoracoabdominal approach with removal of Level III Caval Thrombus)

1. Semi-oblique position
2. 9th intercostal space
3. Carry the incision across the costal margin to the midpoint of the contralateral rectus just above the umbilicus
4. Remove the costal cartilage (tip of 9th and 10th rib)
5. Open the pleura, divide the diaphragm
6. Preserve the phrenic nerve
7. Divide abdominal muscles
8. Enter the peritoneum
9. Cattell-Braasch maneuver
10. Mobilize the kidney
11. Ligate right renal artery
12. Control cava below the right renal vein
13. Control cava above thrombus following mobilization of the liver
14. Control (L) renal vein
15. Remove the caval thrombus and wall of the cava
16. Reconstruct the cava using 3-0 to 5-0 Prolene suture
17. During closure, release distal IVC clamp first, then proximal IVC, then renal vein
18. Close the incision in layers

Note: Consider angioinfarct to obviate need for initial artery ligation. Wait 2–3 days before radical nephrectomy.

Discuss different levels of caval thrombus:

Level I	Perirenal (ostium)	Radical nephrectomy with incision of vena cava
Level II	Infrahepatic	Radical nephrectomy with incision of cava
Level III	Intrahepatic	Suprahepatic IVC control, veno-venous bypass
Level IV	Suprahepatic	Cardiopulmonary bypass/hypothermic arrest (rarely required)
Level IV	Intra-atrial	Cardiopulmonary bypass/hypothermic arrest (rarely required)

Note: Have cardiothoracic surgeon available for tumor thrombus at level II or higher.

Describe surgical management of caval thrombus.

Level I: Thrombus at renal vein ostium:

1. Ligate and divide renal artery and ureter
2. Mobilize the kidney and do not disturb the renal vein or vena cava
3. Place a curved Satinsky around the perirenal vena cava
4. Incise the renal vein
5. Extract the thrombus
6. Repair the vena cava

Level II: Infrahepatic tumor thrombus:

1. Ligate and divide renal artery and ureter
2. Obtain exposure of suprarenal vena cava above the tumor thrombus
3. Secure perforating veins to the caudate lobe of liver as needed
   a. Allows separation of caudate lobe of liver from vena cava
   b. Allows additional 2–3 cm length of vena cava to be exposed
4. Occlude infrarenal vena cava with Satinsky clamp or Rommel tourniquet
5. Secure the opposite renal vein with small bulldog
6. Occlude suprarenal vena cava with Satinsky clamp or Rommel tourniquet
7. Make a circumscribing incision over the tumor thrombus around the renal ostium and vena cava
8. During closure, release distal IVC clamp first, then proximal IVC, then renal vein

Note: Narrowing the vena cava by ≤ 50% does not lead to problems.

Level III: Intrahepatic tumor thrombus:

1. Ligate and divide renal artery and ureter
2. Divide triangular and coronary ligaments
3. Ligate minor hepatic veins
4. Distal control of IVC
5. Control contralateral renal vein
6. Proximal control of IVC above liver but below diaphragm
7. To reduce liver engorgement from back-bleeding:
   a. Pringle maneuver (porta hepatis: portal vein, hepatic artery, bile duct)
   b. Temporarily occlude superior mesenteric artery
   c. Occlusion of porta hepatis and SMA can be safely tolerated for only 20 minutes
8. Remove tumor thrombus
9. During closure, release distal IVC clamp first, then proximal IVC, then renal vein

Note: Consider veno-venous bypass (proximal vena cava to femoral vein) or cardiopulmonary bypass with deep hypothermic circulatory arrest as a useful alternative.

Level IV: Supradiaphragmatic or intra-atrial tumor thrombus:

Cardiopulmonary bypass with/without deep hypothermic circulatory arrest

Can you safely resect infrarenal vena cava for left-sided renal cell carcinoma?

For patients with left-sided tumors and complete occlusion of vena cava, there is minimal risk in resecting infrarenal portion of the cava since adequate collaterals have been established.

What is the collateral circulation for inferior vena cava?

1. Azygous vein (thoracic)—joins vena cava on right side
2. Hemiazygous vein (abdominal)—bilateral
3. Iliolumbar vein
4. Superficial epigastric vein

Can you safely resect suprarenal vena cava for left-sided renal cell carcinoma?

With left-sided tumors, resection of the suprarenal vena cava is not possible due to paucity of collateral venous drainage from the right kidney. In this situation, a tumor-free strip of vena cava must be preserved to provide a right renal venous drainage.

Alternatively, saphenous vein/Gortex graft may be placed from (R) renal vein to vena cava, splenic vein, inferior mesenteric vein, or the portal vein. Otherwise, the right kidney must be auto-transplanted.

Can you safely resect suprarenal vena cava for right-sided renal cell carcinoma?

With right-sided tumors, resection of the suprarenal vena cava is possible provided the left renal vein is ligated distal to the gonadal and adrenal tributaries, which then provide collateral venous drainage from the left kidney.

What is the prognosis for patients with infradiaphragmatic tumor thrombus?

Patients with infradiaphragmatic extension have a prognosis similar to those with lower-stage tumor based on the size of the tumor. Complete surgical extirpation of the tumor is the only hope or treatment for patients without regional or distant metastatic disease.

Only 35% of patients with lymph node involvement survived 2 years after nephrectomy and excision of vena caval thrombus. No patients with distant metastasis survived 3 years after nephrectomy with vena caval thrombus removal. That being said, the survival for untreated caval thrombi is worse, so surgery is still indicated.

What are potential signs and symptoms of renal cell carcinoma?

1. Pain (flank or abdominal)
2. Hematuria
3. Cachexia, weight loss
4. Abdominal mass
5. HTN
6. Classic triad (hematuria, flank pain, mass)
7. Varicoceles of acute onset (usually right side)

Note: A majority of renal masses are now detected incidentally.

What are some systemic manifestations of advanced renal cell carcinoma?

1. HTN → ↑ renin
2. Hypercalcemia → ↑ parathormone like substance
3. Polycythemia → ↑ erythropoietin level
4. Anemia → ↓ erythropoietin level
5. Pyrexia → ↑ IL-1
6. Stauffer Syndrome → non-metastatic hepatic dysfunction; abnormal LFT
   ↓ WBC, fever, liver necrosis without liver metastasis

Note: LFTs return to normal after nephrectomy. Resolution of Stauffer Syndrome is a favorable prognostic sign. Persistent or recurrence of Stauffer Syndrome is associated with tumor recurrence.

7. Cachexia and weight loss
8. Raised alkaline phosphatase

9. Neuromyopathy
10. Amyloidosis
11. Raised ESR

Note: RCC can elaborate a variety of hormones or hormone-like substances such as insulin, glucagon, hCG, prostaglandins, 1,25 dihydroxycholecalciferol, renin, erythropoietin, and parathormone-like factors.

What physical findings may be associated with renal cell carcinoma?

1. Flank mass
2. Pathologic bone fracture
3. Soft tissue and skin nodules
4. Hepatic vein enlargement
5. Acute varicocele that does not collapse on recumbency

What are appropriate diagnostic studies for renal cell carcinoma?

1. CT scan of abdomen
    a. Most useful study for initial evaluation of renal mass
2. MRI
    a. Useful for invasion of renal vein or inferior vena cava
    b. Detect level of vena caval thrombus
3. Transesophageal echocardiogram
    a. Useful for evaluation of supradiaphragmatic caval thrombus, especially if MRI contraindicated
    b. Can also be used intraoperatively
4. CT-Angiography
    a. When nephron-sparing approach is to be used for a solitary kidney
    b. When bilateral partial nephrectomy is needed for bilateral RCC
    c. When radical nephrectomy is required on one side and partial on contralateral side in the setting of bilateral RCC

Where does renal cell carcinoma metastasize?

1. Lung → 50%
2. Liver → 33%
3. Bone → 32%
4. Brain → 25%

What are the estimated 5-year survival rates after radical nephrectomy?

Stage I	95%
Stage II	85%
Stage III	60%
Stage IV	20%

CASE 6

HPI: 28-year-old female with abdominal pain and renal mass detected by sonogram. Symptoms present for 1 month and pain stable. No history of stone disease, UTI, hematuria, or trauma.

PMH: none

PSH: none

Allergies: none **Medications:** none

FH: mother died of cancer
SH: (-) tob; (-) ETOH; single
ROS: feels well, neg

PE:

Vitals	T 98.5 P 110 BP 160/92 Wt. 132 hgt. 5'6"
GA	healthy young female, no distress
HEENT	benign
Heart	RRR
Lungs	CTA
Abdomen	soft; nontender, benign exam (-) CVAT
Ext	(-) CCE
Neuro	non-focal
Genital	WNL, without pathologic findings

What initial lab tests do you order?

UA → pH 5 sp gr 1.010 WNL
CBC & Comp → WNL
Pregnancy test → negative

What is your initial work-up?

State that you would obtain a dedicated CT scan of the abdomen and pelvis with and without contrast to evaluate abdominal pain.

CT abd/pelvis: Bilateral cystic and solid enhancing renal masses, largest on left measuring 4.5 cm, right lesions are all cystic and < 3 cm, multiple pancreatic cystic lesions and left adrenal solid mass 2 cm

CRX: Normal

What is your assessment?

Diagnosis: Bilateral renal masses/cysts, adrenal mass and pancreatic lesions
Differential diagnosis: VHL

What are the clinical features of VHL?

1. Kidney tumors (clear RCC, solid and cystic lesions which are lined by clear cells)
2. Adrenal tumors (pheochromocytoma)
3. Pancreatic tumors (islet tumors)
4. CNS tumors (hemangioblastoma)
5. Retinal tumors (angioma)
6. Endolymphatic sac tumors (inner ear)
7. Epididymal cystadenoma in males

What would you do next?

Work-up: genetics, head and spine MRI, fundus exam and possible adrenal imaging.

What additional studies does this patient need?

Adrenal metabolic work-up (plasma free metanephrines, serum potassium and 24 hour urinary cortisol)

What are the treatment options?

Observation
Cystic lesions or small (<3 cm) solid

Surgical intervention

When?	Larger (>3cm) lesions or critical locations
How?	Partial NX or radical NX and rarely bilateral nephrectomy and renal transplant
Adrenalectomy:	Partial vs. total

What is the follow-up?

Risk of recurrence/progression is 100%.
Imaging once yearly with lab work.

What is the genetic basis of VHL?

VHL gene mutation is detected in germ line of affected individuals (Chromosome 3).

What are the familial types of renal cancer?

1. VHL (von Hippel-Lindau disease)
   Histo: clear cell RCC/Gene: VHL gene
2. HPRC (Hereditary papillary renal carcinoma)
   Histo: papillary Type 1 RCC/Gene: Met proto-oncogene
3. BHD (Birt–Hogg-Dubé syndrome)
   Histo: Chromophobe RCC/oncocytoma/Gene: BHD gene
4. HLRCC (Hereditary Leiomyomatosis and renal-cell cancer syndrome)
   Histo: papillary Type 2 RCC/Gene: FH gene
5. TSC1/TSC2 (Tuberous Sclerosis Complex)

Histo: more commonly associated with AMLs, but as patients age, more commonly associated with ccRCC

6. Succinate Dehydrogenase B germline mutations
7. Xp11.2 (TFE3) Translocation tumors
   Associated with aggressive papillary nested/alveolar type tumors in adults that are very aggressive. Also associated with a lesser aggressive form of RCC in children.

What are the clinical features of BHD and HLRCC?

BHD:	Multiple hair follicle tumors, fibrofolliculoma, pulmonary cysts and renal tumors BHD associated renal tumors may be chromophobe renal carcinoma, hybrid oncocytic neoplasms or oncocytoma
HLRCC:	Cutaneous leiomyomas, Type 2 papillary RCC and uterine leiomyomas/ myosarcoma. Affected individuals with HLRCC are characterized by germ line mutation of FH (fumarate hydratase)

What is Bosniak classification of renal cysts?

1. Type I (simple cyst)
   a. Thin and smooth wall
   b. Spherical or ovoid shape
   c. No enhancement
   d. -10 to +20 Hounsfield units
   e. No treatment required
2. Type II (minimally complicated benign cyst)—less than 10% chance of being malignant
   a. Thin line of calcium
   b. Thin septations, no enhancement
   c. Can be a hyperdense cyst
   d. May be observed
3. Type IIf—less than 30% chance of being malignant
   a. Somewhat more complex than II but without the extensive calcification or nodularity of Type III or IV cyst—therefore warranting follow-up
4. Type III (complex cyst)—approximately 50% chance of being malignant
   a. Extensive calcifications
   b. Multiple, irregular, or thick septations with enhancement
   c. Requires excision
5. Type IV (cystic malignant tumor)—90% chance of being malignant
   a. Obvious tumor
   b. Usually warrants radical/partial nephrectomy
   c. Sometimes difficult to distinguish between Type IV cystic RCC and centrally necrotic RCC

CHAPTER 7

TESTICULAR CANCER

ANDREW LEONE, MD
SCOTT GILBERT, MD

CASE 1

HPI: 27-year-old Caucasian male with painful scrotal swelling × 1 week after being kicked in groin 1 week ago. Has history of right sided cryptorchidism. Is sexually active. No urethral discharge.

PMH: (R) cryptorchid testis

PSH: (R) orchiopexy

Allergies: none **Medications:** none

FH: (-) prostate cancer
SH: (-) tob; (-) ETOH
ROS: non-contributory

PE:

Vitals	T 98.6 BP 140/60 P 90 RR 12
GA	WDWN CM INAD w/o any lymphadenopathy
HEENT	benign
Heart	RRR
Lungs	CTA
Abdomen	soft; NT/ND
Flank	benign; no CVA tenderness
GU	normal circumcised phallus; adequate meatus; (R) hemiscrotum enlarged and tender; (+) Prehn's sign; cremasteric reflex normal; (R) testicle difficult to palpate (L) testicle WNL
Prostate	smooth and benign @ 30 g; (-) nodules or induration
Ext	(-) CCE
Neuro	non-focal
Lymph nodes	(-) adenopathy

What initial lab tests do you order?

UA → 2–3 RBC/HPF; 6–10 WBC/HPF; few bacteria
UCx → no growth
Chem 7 → WNL; Cr 1.1 mg/dL
CBC → WNL

What is your differential diagnosis?

Epididymo-orchitis versus testis tumor versus torsion (although unlikely given time-line).

What is your next step?

State that you would obtain scrotal ultrasound with Doppler studies.

Scrotal US with Doppler studies: (R) testis heterogeneous echogenicity; epididymis enlarged; increased blood flow; (L) testis normal

What is your assessment?

He most likely has epididymo-orchitis.

What is your initial treatment?

1. Ceftriaxone × 1 plus Doxycycline 100 mg po BID × 10 days
2. NSAIDS, i.e., Ibuprofen
3. Scrotal support/warm baths
4. Reassess in 3 weeks

Note: Pain is the first symptom that will resolve. Size of the testis/epididymis is the last symptom to disappear.

What are alternative antibiotics you could use in this patient?

Ceftriaxone (Rocephin) IV × 1 plus Azithromycin if unable to tolerate Doxycycline.

How do you treat epididymo-orchitis in men > 35-years-old (or who engage in anal intercourse)?

1. Ceftriaxone and Ciprofloxacin 500 mg po BID × 10 days or
2. Ofloxacin 400 mg po BID × 2–3 weeks

How is epididymitis treated in recently instrumented men (likely caused by enteric organisms)?

Ofloxacin or Levofloxacin.

What are common clinical presentations of testicular carcinoma?

1. Painless testicular enlargement—most common presenting symptom
2. Testicular mass—firm lump or nodule
3. Testicular pain—heaviness, aching sensation, acute pain ~10% of testis tumors
4. Gynecomastia in 5% of men with testis tumors
5. Abdominal mass or pain
6. Respiratory problems

He returns to clinic after 3 weeks. He is happy that his pain has resolved, but the scrotal swelling persists.

Note: You need to see this patient in follow-up. If the patient has persistent scrotal mass after appropriate antibiotic therapy for 3 weeks, you must suspect testicular tumor and repeat the scrotal ultrasound.

What is your next step?

State that you would obtain scrotal ultrasound and tumor markers.

Scrotal ultrasound: 2 cm hypoechoic mass within (R) testis with a reactive hydrocele; (L) testis normal

AFP:	normal	(0–10 ng/mL)
bhCG:	6.0 mIU/mL	(0–3.5 mIU/mL)
LDH:	normal	

PLAP:	normal	(122–236 U/L)

Note: bhCG is elevated, suggesting seminoma or NSGCT.

What is your recommendation?

Recommend radical orchiectomy via inguinal approach.

Note: Recommend sperm banking prior to surgery.

What is the approach and surgical steps of radical orchiectomy?

Inguinal incision.
High ligation of spermatic cord with permanent suture.

He undergoes right radical orchiectomy without complications.

When would you recommend biopsy of the contralateral testis?

1. US abnormal
2. Cryptorchid testis or poor spermatogenesis
3. Marked atrophy (testis volume <12)

5% of patients will harbor TIN (IGCN/CIS) in contralateral testis.

What is your follow-up?

Ask for pathology report.

Pathology: pure seminoma; (-) margins; (-) lymph or blood vessel invasion; involves tunica albuginea

What is his pathologic stage?

pT2NxMx or stage I.

What is your next step?

Obtain follow-up tumor markers and stage the disease.

bhCG: returns to normal in 1 week

Note: Approximately 5–10% of "pure" seminomas produce bhCG, apparently produced by syncytiotrophoblast-like giant cells occurring in some seminomas.

What is the half-life of bhCG, AFP, and LDH?

bhCG 24–26 hours, AFP 5–7 days, LDH 4 days.

When should bhCG be rechecked postoperatively?

Tumor markers normalize in 4 half-lives. Thus, bhCG should normalize in 1 week and AFP in 4 weeks.

What is your next step?

State that you would obtain additional staging work-up with CT scan of abdomen and pelvis and CXR or CT Chest (EAU Guidelines).

CT scan:	(-) mets; (-) retroperitoneal lymphadenopathy
CXR:	normal

Under what circumstances would you obtain a chest CT?

1. If CXR abnormal
2. If CT of abdomen/pelvis abnormal

Note: EUA guidelines recommend up front Chest CT as 10% of cases can have small subpleural nodes only seen on CT scan.

What is his clinical stage?

Clinical stage IB seminoma.

What are your treatment options?

1. Surveillance
    a. Best option for patients with low risk (tumor size <4cm and no rete testis invasion, recurrence as low as 6%)
    b. Require compliance with follow up and possible concern attributed to radiation from surveillance CT scans
2. External beam radiation therapy
    a. Seminoma is very radiosensitive
    b. Rate of long term severe radiation toxicity is <2% (although risk of death from cardiac disease doubled as well as risk of secondary malignancy)
    c. Para aortic field and ipsilateral iliac nodes ("dog-leg" field) 20 Gy in 10 fractions
    d. Relapse rate 1–3%
    e. EORTC 30942 (TE 18)—study compared 30 Gy in 15 fractions to 20 Gy in 10 fractions, 5-year relapse free survival was 95% and 97% respectively with increased immediate toxicity in the higher dose group (after 12 weeks no difference in toxicity)
3. RPLND
    a. Surgery is NOT indicated for stage I seminoma
4. Single dose Carboplatin
    a. Option for patients especially if non-compliant with surveillance
    b. EORTC 30982 compared single dose Carboplatin to 20–30 Gy XRT and found no difference in relapse
    c. Carboplatin short term side effects—thrombocytopenia and GI toxicity

A discussion should be held with the patient regarding risk benefits of all options.

How should a patient be followed on surveillance?

NCCN Guidelines—Clinical Stage I Seminoma: Surveillance after Orchiectomy*

HPI
    Year 1: q 3–6 mo
        2–3: q 6–12 mo
        4–5: 1 × / yr
Abdominal/Pelvic CT

Year 1: at 3, 6 and 12 mo
  2–3: q 6–12 mo
  4–5: q 12–24 mo
Chest X-ray
  If clinically indicated, evaluate symptomatic patients for chest CT with contrast

*Adapted from: NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Testicular Cancer Version 2.2017. © 2016 National Comprehensive Cancer Network, Inc.

He undergoes external beam radiation to para-aortic area and ipsilateral pelvic nodes (approximately 2500 rads over 3 weeks). He does well from this treatment and thanks you.

What is his follow-up after XRT?

NCCN Guidelines—Clinical Stage I Seminoma: Surveillance after Adjuvant Treatment (Chemotherapy or Radiation)*

HPI
  Years 1–2: q 6–12 mo
    3–5: 1 × / yr
Abdominal/Pelvic CT
  Years 1–3: 1 × yr
    4–5: Not needed
Chest X-ray
  If clinically indicated, evaluate symptomatic patients for chest CT

*Adapted from: NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Testicular Cancer Version 2.2017. © 2016 National Comprehensive Cancer Network, Inc.

How do you treat clinical stage IIA seminoma?

1. Traditional approach (preferred)
   a. External beam radiation to para-aortic area and ipsilateral iliac pelvic nodes
   b. 30 Gy
2. Primary chemotherapy
   a. EP × 4 or BEP × 3 for multiple positive lymph nodes

How do you treat clinical stage IIB seminoma?

Primary chemotherapy (preferred).

1. EP × 4 or BEP × 3
2. RT in non-bulky cases include para-aortic and ipsilateral iliac lymph nodes—36 Gy

What determines treatment for clinical stage IIC or III seminoma?

Patients are stratified based on risk, which determines treatment.

1. Good risk
   a. Any primary site
   b. No non-pulmonary visceral metastases
   c. Normal AFP
   d. Any HCG and LDH
2. Intermediate risk

   a. Any primary site
   b. Non-pulmonary visceral metastases present
   c. Normal AFP
   d. Any HCG and any LDH
3. Poor risk
   a. No seminoma patient classified as having poor prognosis

How do you treat a patient with good risk stage IIC or stage III seminoma?

Primary chemotherapy with EP × 4 cycles or BEP × 3 cycles.

How do you treat a patient with intermediate risk stage IIC or stage III seminoma?

Primary chemotherapy with BEP × 4 cycles; also consider inclusion in clinical trial.

How do you manage post-chemotherapy residual mass for seminoma?

1. Most series of resected masses for seminomas have shown fibrosis and necrosis
2. Masses ≤ 3 cm—surveillance
3. Masses > 3 cm—PET scan >6 weeks post chemo, if positive consider RPLND or second line chemo

What are risk factors for testicular carcinoma?

1. Gonadal dysgenesis
2. h/o previous testis tumor
3. CIS or intra-epithelial germ cell neoplasia
4. Cryptorchidism
   a. Intra-abdominal testis → seminoma
   b. Inguinal testis with orchiopexy → non-seminoma
5. HIV infection
6. Family history of testis cancer in father or brother
7. Infertility including Klinefelter's Syndrome
8. Hypospadias

Note: Men with history of cryptorchidism are 10–40 × higher risk for testicular cancer than general population.

Name primary germ cell tumors and non-germ cell tumors:

1. Primary germ cell tumors
   a. Seminoma
   b. Embryonal carcinoma
   c. Teratoma
   d. Choriocarcinoma
   e. Yolk sac tumor
2. Non-germ cell tumors—only 10% malignant, treated with orchiectomy and surveillance
   a. Leydig cell tumor
   b. Sertoli cell tumor

What is the relative frequency of primary germ cell tumors?

1. Seminoma	60%
2. Embryonal carcinoma	20%

3. Teratocarcinoma	15%
4. Teratoma	5%
5. Choriocarcinoma	1%
6. Yolk sac tumor	< 1%

Note: Yolk sac tumor usually is not a sole or predominant cell type in the adult population.

How does testicular carcinoma spread locally?

Rete testis epididymis spermatic cord.

How does testicular carcinoma spread systemically?

Testicular cancers spread primarily via lymphatic circulation:

1. Retroperitoneal nodal metastasis
2. Cisterna chyli
3. Thoracic duct
4. Supradiaphragmatic nodes
5. Extra nodal/distant metastasis
6. Exception is choriocarcinoma (+ yolk sac) with demonstrate hematogenous spread

What is the pattern of nodal spread for testicular cancer?

1. Right testis tumor
   Interaortocaval → precaval → preaortic → paracaval → right → common iliac→ right external iliac
2. Left testis tumor
   Para-aortic → preaortic → left common iliac → left external iliac → interaortocaval → precaval → paracaval

   Lymphatic spread goes from right to left in the retroperitoneum but rarely the converse

How do you manage carcinoma-in-situ?

Treatment dependent on status of contralateral testis.

1. Management is controversial with no quality evidence available and includes:
   a. Orchiectomy in men with well-functioning contralateral testis
   b. Low dose radiation (18–20 Gy)
   c. Close surveillance in solitary testis
2. Important to note that 30% of CIS progress to clinically invasive disease

Discuss the TNM and American Joint Committee Staging System for Testis Cancer:

Testis Cancer (TNM and American Joint Committee Classification):

Tx	Cancer stage unknown
To	No evidence of cancer
pTis	Intratubular germ cell neoplasia (carcinoma in situ)
T1	Tumor limited to testis and epididymis **without** vascular/lymphatic invasion; tumor may invade into the tunica albuginea but not the tunica vaginalis

T2	Tumor limited to testis and epididymis **with** vascular/lymphatic invasion, or tumor extending though the tunica albuginea with involvement of the tunica vaginalis
T3	Tumor invades the spermatic cord with or without vascular/lymphatic invasion
T4	Invasion of the scrotum
Tx	Nodal involvement unknown
No	No evidence of nodal involvement
N1	Single node or nodes < 2 cm
N2	Single node or nodes (2–5 cm)
N3	Single node or nodes > 5 cm
Mx	Distant metastasis unknown
Mo	No evidence of distant metastasis
M1	Distant metastasis present
SX	Marker studies not available or not performed
S0	Marker study levels within normal limits
S1	LDH < 1.5 × normal and HCG < 5000 and AFP < 1000
S2	LDH 1.5–10 × normal or HCG 5000–50,000 or AFP 1000–10,000
S3	LDH > 10 × normal or HCG > 50,000 or AFP> 10,000

Stage 0	pTis	N0	M0	S0
Stage I	pT1–4	N0	M0	SX
Stage IA	pT1	N0	M0	S0
Stage IB	pT2	N0	M0	S0
	pT3	N0	M0	S0
	pT4	N0	M0	S0
Stage IS	any T	N0	M0	S1–3
Stage II	any pT	N1–3	M0	SX
Stage IIA	any pT	N1	M0	S0
	any pT	N0	M0	S1
Stage IIB	any pT	N2	M0	S0
	any pT	N2	M0	S1
Stage IIC	any pT	N3	M0	S0
	any pT	N3	M0	S1
Stage III	any pT	any N	M1	SX
Stage IIIA	any pT	any N	M1	S0 or S1
Stage IIIB	any pT	N1–3	M0	S2
	any pT	any N	M1	S2
Stage IIIC	any pT	N1–3	M0	S3
	any pT	any N	M1	S3

Republished with permission of Springer-Verlag New York Inc, from AJCC Cancer Staging Manual, Edge SB, 7th ed. ©2009; permission conveyed through Copyright Clearance Center, Inc.

CASE 2

HPI: 21-year-old Caucasian male complaining of progressively worsening right scrotal swelling × 2 weeks. He states that he was kicked in the groin 1 week ago and history of right sided cryptorchidism.

PMH: none

PSH: (R) hernia repair

Allergies: none **Medications:** none

FH: (-) prostate cancer
SH: (-) tob; (-) ETOH
ROS: non-contributory

PE:

Vitals	T 98.6	BP 140/60	P 90	RR 12
GA	WDWN CM INAD w/o any lymphadenopathy			
HEENT	benign			
Heart	RRR			
Lungs	CTA			
Abdomen	soft; NT/ND			
Flank	(-) CVAT			
GU	normal circumcised phallus; adequate meatus; (R) hemiscrotum enlarged; 10 cm firm mass; (R) testicle difficult to palpate; (R) testis indistinguishable from epididymis; (-) Prehn's sign; cremasteric reflex normal; (L) testicle WNL			
Prostate	smooth and benign @ 30 g; (-) nodules or induration			
Ext	(-) CCE			
Neuro	non-focal			

What initial lab tests do you order?

UA → WNL
UCx → no growth
CBC → WNL
Chem 7 → WNL; Cr 1.0 mg/dL

What is your differential diagnosis?

Trauma versus epididymo-orchitis versus testis tumor.

What is your next step?

State that you would obtain scrotal ultrasound and tumor markers.

Scrotal US with Doppler studies: (R) testis heterogeneous echogenic 10 cm mass;
(+) microlithiasis;
(L) testis normal except for microlithiasis

AFP:	5.0 ng/mL	(0–10.0 ng/mL)
bhCG:	600 mIU/mL	(0–3.5 mIU/mL)
LDH:	300 U/L	(122–236 U/L)

bhCG and LDH levels are elevated.

Note: LDH levels correlate with tumor bulk in NSGCT tumor burden.

What is your assessment?

Testicular tumor.

What is your initial treatment?

Recommend radical orchiectomy via inguinal approach.

Note: Recommend sperm banking prior to surgery.

He undergoes radical orchiectomy without complications.

What is your follow-up?

Ask for pathology report. Better yet, state that you would review the pathology specimen with the pathologist. In addition, obtain follow-up tumor markers.

Pathology:	embryonal and teratoma; (-) margins; involves rete testis and epididymis; (+) lymph or blood vessel invasion
LDH:	returns to normal

What is his pathologic stage?

pT3NxMx or stage I

What is your next step?

State that you would obtain additional staging work-up with CT scan of abdomen and pelvis and CXR.

CXR:	5 mm nodule
CT scan:	(-) mets; (-) retroperitoneal lymphadenopathy

When is brain MRI or bone scan indicated?

When clinical signs or symptoms are present.

What do you do next?

Chest CT to further evaluate the pulmonary nodule; also obtain former CXRs of the patient if available for comparison.

Chest CT:	5 mm nodule (unclear whether this is granuloma or tumor); may perform FNA; if FNA non-diagnostic, perform biopsy
FNA:	equivocal

Because the FNA was equivocal, he underwent video-assisted thoracoscopic biopsy of the lesion. The lesion was benign granuloma.

What is his clinical stage?

Clinical stage IB NSGCT

What are your treatment options?

1. Surveillance
   a. Only for T2
   b. Patient also needs to be very compliant with rigorous surveillance regimen; NOT the best option for this patient
   c. >50% embryonal may increase risk of relapse and make surveillance an inferior treatment option
   d. LVI most important factor to predict occult metastases
   e. SWENOTECA trial, all men stage I NSGCT no LVI underwent surveillance, compared surveillance to BEP × 1, BEP × 2, recurrence rate 12%, 1%, 0%
2. Chemotherapy
   a. 1 cycle of BEP or 2 cycles is an option (teratoma is resistant to chemotherapy), risk of infertility, secondary cancer, cardiac disease
3. Nerve-sparing Retroperitoneal Lymph Node Dissection (NS-RPLND)
   a. This is another treatment option for him
   b. Note that RPLND is appropriate for stage I and IIA disease
4. Radiation
   a. This is non-seminomatous germ cell tumor
   b. Radiation is contraindicated for this patient

He opts for RPLND after a lengthy discussion.

What is his probability of having teratoma on RPLND?

Approximately 2–19%, even without teratoma in orchiectomy specimen, 5–7% risk of teratoma in RP.

How do you proceed?

Obtain informed consent. Get preoperative labs. Bowel prep the patient with mechanical and antibiotic bowel prep. T&C 2 units. Give preoperative antibiotics and SCD.

What type of RPLND does he need?

Nerve-sparing RPLND.

What is the difference between standard, limited, and nerve-sparing RPLND?

1. Standard RPLND
   a. Historically, the standard RPLND included a full bilateral dissection from above the renal vein to below the aortic bifurcation. Anejaculation approached 100% since sympathetic ganglia were routinely sacrificed
      i. Full bilateral left-sided dissection
         Superior: (L) adrenal, renal veins, below SMA
         Inferior: aortic bifurcation; IMA is sacrificed
         Medial: medial to (R) ureter

        Lateral: (L) renal hilum, ureter, iliac bifurcation

    ii. Full bilateral right-sided dissection
        Superior: (R) adrenal, renal veins, below SMA
        Inferior: aortic bifurcation; IMA is sacrificed
        Medial: medial to (L) ureter
        Lateral: (R) renal hilum, ureter, iliac bifurcation

2. Limited RPLND
   a. In this setting, the area overlying the aorta below IMA is spared. Because postganglionic sympathetic fibers are preserved, ejaculation is preserved in 80–90% patients
      i. Limited left-sided dissection
         Superior: (L) adrenal, (L) renal vein, below SMA
         Inferior: above IMA (IMA is spared)
         Medial: mid-vena cava
         Lateral: (L) renal hilum, ureter, iliac bifurcation
      ii. Limited right-sided dissection
         Superior: (L) adrenal, renal veins, below SMA
         Inferior: above IMA (IMA is spared)
         Medial: lateral to aorta
         Lateral: (L) renal hilum, ureter, iliac bifurcation
3. Nerve-sparing RPLND
   a. This technique preserves branches of sympathetic chain that course over the aorta
   b. Preservation of ejaculation approaches 100% using this technique
   c. This technique is not routinely recommended for patients with grossly positive nodes
   d. Nerve sparing RPLND is usually performed in combination with limited dissection

Describe the surgical technique:

Either thoracoabdominal or transabdominal approaches may be used. In this case, transabdominal incision was executed. Place NGT and Foley catheter.

The Operation (RPLND—Transabdominal Approach)

1. Midline incision from xiphoid to below umbilicus
2. Incise white line of Toldt in (R) paracolic gutter
3. Mobilize (R) colon and cecum up to the ligament of Treitz
4. IMV can be routinely divided to facilitate mobilization of the left colon mesentery if necessary
5. Modified nerve-sparing template
   a. Right side
      i. Ureter, renal vein, lateral wall of the aorta, IMA, iliac bifurcation
      ii. It is important to include the interaortocaval area
   b. Left side
      i. Ureter, renal vein, mid wall of vena cava, IMA, iliac bifurcation
      ii. It is important to include the interaortocaval area
6. Use split and roll technique
7. Spare the nerves
   a. L1, L2, L3, L4
      i. L3 is most important for ejaculation
   b. Identify the postganglionic nerve fibers overlying the anterior aorta arising from bilateral sympathetic chains
   c. Sympathetic chains are identified just above the common iliacs

   d. Nerves course anterior to the aorta and interaortocaval area and dip behind the vena cava
   e. Identify lumbar veins as a landmark. Ligate and divide lumbar arteries and veins because nerves are very close to these structures
8. Dissect out the ipsilateral spermatic cord
9. Close the incision

During the operation, you encounter enlarged or indurated nodes. The nodes are 1.5 cm in diameter.

What percentage of patients will be upstaged to pathologic Stage II?

30% of patients.

What is the clinical stage and what do you do?

Presence of lymph nodes < 2 cm indicates he has Stage IIA disease.

Presence of enlarged or indurated lymph nodes are indicative of Stage II disease. In questionable cases, intraoperative frozen section is performed to confirm tumor. Whether or not to extend the limits of dissection is determined by the location of the tumor.

If lymph nodes are grossly positive (stage IIB: > 2 cm, < 5 cm), bilateral suprahilar dissections should be performed routinely. The dissection should extend 4–6 cm above renal arteries to expose the crura of the diaphragm. Head and body of the pancreas are retracted cephalad. IMV is ligated. SMA is identified and preserved. Cisterna chyle is clipped. Limits of dissection include: first hepatic vein (vena cava)—superiorly, renal arteries—inferiorly, medial aspect of adrenal glands—laterally.

If the nodes are near the origin of IMA, extend the dissection over the lower aorta and down the contralateral common iliac artery. If this is not done, retrograde lymphatic spread of the tumor can occur since these nodes are obstructed by the tumor.

If the nodes are located superior to IMA, the lower aorta may be preserved. The limits of dissection include contralateral ureter with complete mobilization of the aorta and vena cava. The main sympathetic ganglia should be preserved unless adenopathy is adherent to psoas muscle and vertebral bodies.

Note: Approximately 10% of patients with negative CT scan and tumor markers are found to have grossly positive nodes at the time of RPLND. When stage II disease is encountered, RPLND must be extended to full bilateral dissection.

What are potential intraoperative/postoperative complications?

1. Vena cava laceration
   a. Proximal and distal control
   b. Oversew with 4-0 Prolene
   c. If unable to control bleeding, hold pressure on vessel and consult vascular surgery
2. IMA injury
   a. It is generally okay to ligate IMA (if necessary) since there is collateral circulation with marginal artery of Drummond
   b. However, IMA is not routinely ligated during uneventful RPLND

Note: IMA supplies distal half of transverse colon, descending colon, sigmoid and rectum. SMA supplies proximal half of transverse colon, ascending colon, and small bowel.

3. Cisterna chyle laceration
   a. Located on right side of L1-L2 vertebrae
   b. Ligate cisterna chyle if recognized intraoperatively
   c. Unrecognized cisterna chyle injuries present with chylous ascites

Chylous ascites → diagnose by paracentesis; treat with NPO, TPN, or low fat, high protein, medium chain triglycerides (MCT) diet, possible drainage or somatostatin analogues

Patient is tachycardic postoperative to the 120s–130s.

What would you do?

Perform EKG, assess fluid status urine output.

Postoperative tachycardia is common, caused by sympathetic discharge (~2%).

Note: Important to distinguish from hypovolemia.

He tolerated the procedure without complications and was transferred to the PACU. He had benign postoperative course. He was discharged to home several days later.

What do you do now?

You should ask for the pathology report.

Pathology report: 2 lymph nodes (< 2 cm) positive for embryonal carcinoma; (+) teratoma

What is his pathologic stage?

pT3N1Mx or stage IIA NSGCT

What do you recommend?

Surveillance (preferred) or Chemotherapy (2 cycles of BEP).

You obtained medical oncology consult. After extensive counseling, the patient elects to undergo 2 cycles of BEP.

What is BEP and its complications?

Bleomycin, Etoposide, and Cisplatin.

Bleomycin	pulmonary toxicity
Etoposide	myelosuppression
Cisplatin	renal toxicity

Note: Other complications include peripheral neuropathy, Raynaud's phenomenon, and azoospermia, ototoxicity, cardiac toxicity.

What is your follow-up?

NCCN Guidelines—Stage IIA/B NSGCT Post Primary RPLND and NOT Treated with Adjuvant Chemotherapy*

- HPI and tumor markers
  - Year 1: q 2 mo
  - 2: q 3 mo
  - 3: q 4 mo
  - 4: q 6 mo
  - 5: 1 × yr
- Abdominal/Pelvic CT
  - Year 1: At 3–4 mo
  - 2–5: As clinically indicated
- Chest x-ray
  - Year 1: q 2–4 mo
  - 2: q 3–6 mo
  - 3–5: 1 × / yr

*Adapted from: NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Testicular Cancer Version 2.2017. © 2016 National Comprehensive Cancer Network, Inc.

What is the surveillance protocol for Stage IA NSGCT?

NCCN Guidelines—Stage IA, NSGCT: Active Surveillance*

- HPI and tumor markers
  - Year 1: q 2 mo
  - 2: q 3 mo
  - 3: q 4–6 mo
  - 4: q 6 mo
  - 5: 1 × / yr
- Abdominal/Pelvic CT
  - Year 1: q 4–6 mo
  - 2: q 6–12 mo
  - 3: q yr
  - 4–5: Not indicated
- Chest X-ray
  - Year 1: At mo 4 and 12
  - 2–5: 1 × / yr

*Adapted from: NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Testicular Cancer Version 2.2017. © 2016 National Comprehensive Cancer Network, Inc.

What is the surveillance protocol for Stage IB NSGCT?

NCCN Guidelines—Stage IB, NSGCT: Active Surveillance*

- HPI and tumor markers
  - Year 1: q 2 mo
  - 2: q 3 mo

3: q 4–6 mo
4: q 6 mo
5: 1 × / yr

Abdominal/Pelvic CT
Year 1: q 4 mo
2: q 4–6 mo
3: q 6 mo
4: 1 × /yr
5: Not indicated

Chest x-ray
Year 1: q 2 mo
2: q 3 mo
3: q 4–6 mo
4: q 6 mo
5: 1 × / yr

*Adapted from: NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Testicular Cancer Version 2.2017. © 2016 National Comprehensive Cancer Network, Inc.

AFP level is elevated in what conditions?

1. Elevated in hepatoma, pancreas carcinoma, brochogenic carcinoma
2. Elevated in fetal yolk sac tumor, embryonal carcinoma, teratocarcinoma
3. Should not be elevated in pure seminoma or choriocarcinoma
4. Elevated in infants <1-year-old
5. Liver dysfunction, i.e., hepatitis, cirrhosis

bhCG level is elevated in what conditions?

1. Elevated in choriocarcinoma, seminoma, teratocarcinoma, embryonal carcinoma
2. Chain cross reacts with FSH, LH, and TSH
3. Also elevated in marijuana users

LDH level is elevated in what conditions?

1. Elevated in both seminomas and non-seminomas
2. Isoenzyme-1 is most useful
3. Useful for monitoring treatment in seminomas and nonseminomas when AFP and bhCG have normalized
4. Useful for "bulky" seminomas
5. Not routinely used as a tumor marker

What is the cure rate for pathologic stage I NSGCT after RPLND alone?

1. Cure rate is approximately greater than 90%
2. The remaining relapse will likely have recurrence at distant sites (lung)
3. Patients who relapse will have high cure rate with salvage chemotherapy
4. Those who relapse will do so usually within first 2 years after RPLND
5. Although relapse beyond 2 years is rare, patients should be followed annually for next several years

CASE 3

HPI: 32-year-old Caucasian male complaining of progressive, painless right scrotal swelling × 3 months. No fevers, urethral discharge, or trauma.

PMH: none

PSH: none

Allergies: none **Medications:** none

FH: (-) prostate cancer
SH: (-) tob; (-) ETOH
ROS: non-contributory

PE:

Vitals	T 98.6	BP 140/60	P 90	RR 12
GA	WDWN CM INAD w/o any lymphadenopathy			
HEENT	benign			
Heart	RRR			
Lungs	CTA			
Breasts	bilateral gynecomastia			
Abdomen	soft; NT/ND			
Flank	(-) CVAT			
GU	normal uncircumcised phallus; adequate meatus; (R) hemiscrotum enlarged; 6 cm firm mass; (R) testis indistinguishable from epididymis; (-) Prehn's sign; cremasteric reflex normal; (L) testicle WNL			
Prostate	smooth and benign @ 25 g; (-) nodules or induration			
Ext	(-) CCE			
Neuro	non-focal			
Lymph nodes	(-) palpable adenopathy			

What initial lab tests do you order?

UA → WNL
UCx → no growth
CBC → WNL
Chem 7 → WNL; Cr 0.8 mg/dL

What is your differential diagnosis?

Epididymo-orchitis versus testis tumor.

Although differential diagnosis of any testis enlargement includes all of above, he most likely has testis tumor. In the absence of pain, epididymo-orchitis and torsion are not likely diagnoses.

What is your next step?

State that you would obtain scrotal ultrasound and tumor markers.

Scrotal ultrasound: (R) testis heterogeneous echogenic 6 cm mass; (L) testis normal

AFP:	70.0 ng/mL	(0–10.0 ng/mL)
bhCG:	65.0 mIU/mL	(0–3.5 mIU/mL)
LDH:	500 U/L	(122–236 U/L)

What is your impression?

In the setting of testis tumor and elevated tumor markers, he may have NSGCT with metastasis.

What is your recommendation?

Recommend radical orchiectomy via inguinal approach.

Note: Recommend sperm banking prior to surgery.

He undergoes uncomplicated right radical orchiectomy.

What is your follow-up?

Ask for pathology report.

Pathology: choriocarcinoma, yolk sac, and teratoma elements; (-) margins; involves spermatic cord; (+) lymph or blood vessel invasion

What is his pathologic and clinical stage?

He has pathologic stage pT3NxMx3 or clinical stage IB at this point.

What is your next step?

State that you would obtain additional staging work up with CT scan of abdomen and pelvis.

CXR: normal
CT scan: 6 cm interaortocaval lymphadenopathy

What do you do now?

Obtain a CT scan of the chest (given the presence of bulky retroperitoneal disease).

CT scan of chest: Normal

What is his clinical stage now?

He has clinical stage T3N3Mo3 or Stage IIC at this point.

Now what is your next step?

Obtain post-orchiectomy tumor markers at 4 weeks.

AFP:	2500
bHCG:	11,450
LDH:	1500

Note: Always obtain post-orchiectomy tumor markers.

What are his treatment options?

1. Surveillance
    a. This is not an acceptable answer. He has bulky retroperitoneal disease with persistently elevated tumor markers
    b. You must treat this disease aggressively
2. RPLND
    a. Although RPLND may still be possible technically, this patient has elevated tumor markers. This suggests he has metastatic disease that cannot be cured by RPLND alone
    b. After his RPLND, his disease will continue to progress. At this point, you must offer him chemotherapy
    c. You will lose points if you follow this protocol
3. Chemotherapy
    a. This is the best answer. You must give him primary chemotherapy since his markers are still elevated after orchiectomy
    b. However, he may also need adjuvant RPLND (after his markers normalize) since there is teratoma element in the primary specimen

He agrees to receive chemotherapy.

What do you recommend?

4 cycles of Bleomycin, Etoposide, and Cisplatin.

He receives chemotherapy (BEP × 4 cycles).

What guides the number of cycles a patient with stage IIC disease receives?

Patients with stage IIC non-seminoma (NSGCT) can be risk stratified based on their tumor markers.

1. Good risk:
    a. All tumor markers, AFP < 1000, HCG < 5000, LHD < 1.5 × normal (S0 or S1)
    b. Treat with EP × 4 cycles or BEP × 3 cycles
2. Intermediate risk:
    a. Any tumor markers: AFP 1000–10,000, HCG 5000–50,000, LDH 1.5–10 × normal (S2)
    b. Treat with BEP × 4 cycles
3. High risk
    a. Any tumor markers: AFP > 10,000, HCG > 50,000, LDH > 10 × normal (s3)
    b. Mediastinal primary tumor
    c. BEP × 4 cycles or VIP × 4

What is your follow-up?

You repeat the tumor markers and obtain CT scan of abdomen.

AFP:	normal
bHCG:	normal
LDH:	normal
CT scan:	2 cm residual mass in interaortocaval area

Can imaging modalities distinguish between fibrosis/necrosis and malignancy or teratoma?

No, CT cannot reliably distinguish.

What is your impression and recommendation?

His tumor has shrunk nicely with chemotherapy, and his tumor markers have normalized. The residual mass may still harbor testis cancer so he needs post-chemotherapy RPLND.

What is your next step?

Obtain informed consent. Obtain preoperative labs. Bowel prep the patient with mechanical and antibiotic bowel prep. T&C 2 units. Give preop antibiotics and SCD.

Remember that he has received chemotherapy. Use room air FIO2 and be judicious with fluids. Discuss with anesthesiology preoperatively about the need for low inspired oxygen level and low crystalloid replacement during the perioperative period.

Describe the procedure:

Patients with significant retroperitoneal tumor involvement are best approached via thoracoabdominal incision. However, transabdominal approach may be used in patients with minimal disease, such as this patient.

The Operation (Post-chemo RPLND)

1. Midline incision
2. Incise white line of Toldt in (R) paracolic gutter
3. Mobilize (R) colon and cecum up to the ligament of Treitz
4. Identify SMA and preserve it
5. Identify the tumor mass
6. Mobilize (L) colon and sigmoid mesentery
7. Dissect out both ureters, renal veins, and renal arteries
8. Ligate gonadal vessels bilaterally
9. Ligate all lumbar arteries and veins below the renal vessels
10. Dissect out the tumor
    a. Divide the tumor mass over the aorta and vena cava
    b. Find a plane between the fibrous capsule of the tumor and anterior wall of the great vessels
    c. In case of large mass, no attempt is made to spare the nerves
    d. Perform suprahilar dissection if there is any question of retrocrural involvement
11. Do not ligate lumbar vessels above the renal hilum
    a. There is risk of devascularizing the spinal cord

12. Ligate the thoracic duct and the hemiazygous vein as needed on the right side
13. Remove the mass
14. Check for hemostasis and close the incision

What is the likelihood of finding cancer in this setting?

Resected mass may be cancer, teratoma, or scar.

Persistent cancer	20%
Mature or immature teratoma	40%
Fibrosis and necrosis	40%

Note: If persistent carcinoma is present, further courses of chemotherapy should be given.

What are potential complications and treatment of RPLND?

1. Adult respiratory distress syndrome (ARDS)
    a. ARDS associated with bleomycin toxicity is often fatal
    b. Risk of ARDS increases with increased FIO2 and **overhydration**
    c. Ventilate patients with room air oxygen and do not increase FIO2 greater than 25–30%
    d. Use colloid-to-crystalloid ratio of 2:1 during the perioperative period
    e. If volume needed, preferred red blood cell transfusion to crystalloid
2. Mass invades duodenum
    a. Perform partial duodenal resection
3. IMA is encased by the tumor
    a. Divide the IMA as long as marginal artery remains intact
4. Ureter is completely encased or directly invaded by the tumor
    a. Perform nephroureterectomy
5. Tumor invades the aorta, vena cava, or iliac vessels
    a. Excise and replace affected vessels or perform vascular patch graft
6. Psoas muscle is involved by the tumor
    a. Resect the psoas fascia and the involved muscle
7. Tumor thrombus is present in the vena cava below the renal veins
    a. Ligate the vena cava below the renal veins
    b. Patients will develop lower extremity edema, but it will resolve
8. Tumor invades the wall of the vena cava below the renal veins
    a. Ligate the vena cava below the renal veins
    b. Patients will develop lower extremity edema, but it will resolve
9. Sigmoid mesentery is adherent to the mass
    a. Resect the mesentery and mesenteric vessels
    b. Make sure marginal artery and vein remain intact

He undergoes a difficult RPLND but does well postoperatively and is discharged to home a few days later.

What do you do now?

Ask for pathology report.

Pathology report: residual mass positive for embryonal carcinoma and teratoma

What is your next step?

Oncology consult and salvage chemotherapy.

What chemotherapy regimens are used in the salvage setting?

1. VP-16, Ifosfamide, Cisplatin (VeIP)
   a. Approximately 30% durable responses in salvage setting
   b. Patients should receive MESNA before beginning Ifosfamide to prevent hemorrhagic cystitis
2. Paclitaxel/Ifosfamide/Cisplatin (TIP)
   a. Approximately 25% durable response rates
   b. Patients should receive MESNA before beginning ifosfamide to prevent hemorrhagic cystitis
3. Gemcitabine/Ifosfamide/Cisplatin
   a. Small study reporting a 54% complete response rate (Ann Oncol 2014;25(5):987–91)
4. High dose chemotherapy with autologous peripheral blood derived stem cell support
   a. Indicated in unfavorable prognosis group (incomplete previous response, high markers, high volume, extratesticular primary, late relapse)
   b. 2 cycles of high dose Carboplatin plus Etoposide, with or without Cyclophosphamide (or Ifosfamide), result in durable responses in up to 20% of patients
   c. Alternative: clinical trial enrollment

What is your follow-up?

1. CXR and markers Q 3 months × 2 years, then Q 6 months × 3 years
2. CT scan (abdomen and pelvis) Q 6 months

How do you manage post-chemotherapy residual mass for NSGCT?

1. Residual mass should be excised as completely as possible (in contrast to seminoma) in all patients with mass >1cm short axis
2. Timing of post-chemotherapy RPLND is extremely important
3. Markers must have normalized before RPLND is undertaken
4. If markers are persistently elevated, further chemotherapy is indicated

CASE 4

HPI: 35-year-old Caucasian male with progressive, painless scrotal swelling × 5 months. He underwent right orchidopexy at age 2 for undescended testicle.

PMH: (R) cryptorchid testis

PSH: (R) orchiopexy

Allergies: none **Medications:** none

FH: (-) prostate cancer
SH: (-) tob; (-) ETOH; college student
ROS: non-contributory

PE:

Vitals	T 98.6	BP 120/60	P 80	RR 16
GA	WDWN CM INAD			
HEENT	benign			
Heart	RRR			
Lungs	CTA			
Abdomen	soft; NT/ND			
Flank	benign			
GU	normal circumcised phallus; adequate meatus; (R) hemiscrotum enlarged and nontender; (-) transillumination, (R) testicle difficult to palpate; (L) testicle WNL; cord structures normal			
Lymph nodes	(-) palpable adenopathy; esp. supraclavicular and inguinal			
Prostate	smooth and benign @ 25 g			
Ext	(-) CCE			
Neuro	non-focal			

What initial lab tests do you order?

UA → WNL
CBC → WNL
Chem 7 → WNL

What special labs do you order?

You must obtain serum tumor markers

AFP:	70.0 ng/mL	(0–10.0 ng/mL)
bhCG:	2.3 mIU/mL	(0–3.5 mIU/mL)
LDH:	normal	

What is your differential diagnosis?

Scrotal mass with elevated tumor markers. State that you would obtain scrotal ultrasound.

Scrotal ultrasound:	(R) testis heterogeneous echogenicity; epididymis normal; small hydrocele; (L) testis normal

Note: If clinical examination is classic for testicular tumor, scrotal US is not necessary. However, scrotal US allows you to evaluate contralateral testicle prior to radical orchiectomy.

What is your assessment?

Testicular tumor.

What is your recommendation?

Recommend radical orchiectomy via inguinal approach.

Note: Recommend sperm banking prior to surgery.

At the time of orchiectomy, the testicle appears to be fixed to the scrotal wall.
Your partner decides to remove the tumor through a scrotal incision as opposed to inguinal incision.

He undergoes uneventful recovery.

Note: Trans-scrotal biopsy or trans-scrotal orchiectomy in the setting of testicular tumor should not be done.

What is your follow-up?

Ask for pathology report. In addition, obtain follow-up tumor markers 4 weeks after orchiectomy.

Pathology: pure seminoma (classic); (+) margins with involvement of rete testis, spermatic cord, and the scrotal wall; (+) lymphatic and blood vessel invasion

AFP:	7.0 ng/mL	(0–10.0 ng/mL)
bhCG:	2.2 mIU/mL	(0–3.5 mIU/mL)

Note: Half-life of bhCG is 24–36 hours and AFP is 5–7 days.

What is the pathologic and clinical stage?

Pathologic stage pT4NxMx
Clinical stage I seminoma

Note: This patient had elevated AFP before radical orchiectomy. The pathology specimen does not corroborate this finding. Pure seminoma does not cause elevation of AFP. Do not make the diagnosis of seminoma in face of AFP elevation. AFP is produced only by embryonal or yolk sac elements.

What do you do about this discrepancy?

State that you would obtain a second opinion or go over the specimen with the pathologist.

The specimen was carefully step sectioned. The final pathology revealed areas of classic seminoma as well as embryonal carcinoma and yolk sac tumor.

What is your next step?

State that you would obtain additional staging work-up with CT scan of abdomen and pelvis and CXR.

CT scan:	(-) mets; (-) retroperitoneal lymphadenopathy
LFTs:	normal
CXR:	normal

What is your assessment?

Clinical stage IB NSGCT.

What are your treatment options?

1. Chemotherapy
    a. Platinum based chemotherapy (e.g., BEP × 1 or 2 cycles) is best treatment, compared to primarily RPLND BEP × 1, 7% in favor of chemo
2. Nerve-sparing RPLND
    a. 1 of 2 possibilities
        i. Primary landing sites for (R) sided tumors interaortocaval → precaval → (R) iliac
        ii. Primary landing sites for (L) sided tumors paraaortic → preaortic
        iii. Nerve-sparing technique achieves antegrade ejaculation in most patients. You must prospectively identify and preserve sympathetic trunks (L1–4) as they course posterior to the IVC on the right and anterior to the aorta on the left, they coalesce just inferior to IMA at inferior hypogastric plexus
3. Surveillance
    a. This patient has T4 disease and is not a candidate for surveillance

You discuss the pros and cons of each protocol, and patient opts for RPLND.

Note: Since this is a testicular tumor and the scrotum has been violated at the time of orchiectomy, address the treatment of scrotal violation/contamination.

What are treatment options for scrotal tumor contamination?

1. Stage I pure seminoma
    a. Extend retroperitoneal radiation to include ipsilateral hemiscrotum and inguinal nodes
    b. Risk of subsequent azoospermia should be discussed
2. Stage I NSGCT
    a. Widely excise previous scrotal scar and spermatic cord at the time of RPLND
    b. If RPLND is not planned, widely excise the scrotal scar and spermatic cord as a separate procedure

    c. Perform formal hemiscrotectomy in case of gross contamination, will not eliminate risk of relapse
3. Advanced disease treated with full-dose platinum chemotherapy
    a. No additional treatment needed. Examine inguinal nodes at scheduled visits

After discussing with the patient, you decide to widely excise previous scrotal scar at the time of RPLND.

How does trans-scrotal orchiectomy affect local recurrence rates and overall survival (OS)?

Increases local recurrence, but no change in OS.

How do you proceed?

Obtain informed consent, discuss sperm banking if it was not done already, obtain preoperative labs and T&C blood, and give preoperative antibiotics.

Discuss your surgical technique:

The Operation (RPLND and Partial Scrotectomy)

1. Transabdominal approach
2. Reflect colon
3. "Split and roll" technique
4. Remove the spermatic cord
5. Excise (R) hemiscrotum
6. Lymph nodes were enlarged
7. Intraoperative frozen section revealed positive nodes
8. You converted to full bilateral template approach

He underwent uneventful surgery.

What is your next step?

Check pathology report.

Pathology: of the lymph nodes, 7 out of 12 are positive for embryonal carcinoma. Positive lymph nodes measure 4 cm in diameter

What is his pathologic stage?

pT4bN2Mx or pathologic stage IIB NSGCT.

What is your recommendation?

1. Adjuvant chemotherapy
    a. Preferred approach is to give chemotherapy, i.e., EP × 2 cycles or BEP × 2 cycles
2. Observe
    a. Not advised in this patient even if he is highly compliant, given his p4N2 embryonal cancer

State that you would give adjuvant chemotherapy.

You would give 2 cycles of BEP.

Complications of BEP:

Bleomycin	pulmonary toxicity
Etoposide	myelosuppression
Cisplatin	renal toxicity

Note: Approximately 50% relapse if adjuvant platinum-based chemotherapy is not used in this setting.

What is your follow-up?

1. CXR and markers Q 3 months × 2 years, then Q 6 months × 3 years
2. CT scan (abdomen and pelvis) Q 6 months

Define clinical stage IIA and IIB.

Patients are determined to be clinical stage IIA or IIB when tumor markers remain elevated after orchiectomy or if they have retroperitoneal adenopathy on CT scan (refer to tumor staging).

What are treatment options for clinical stage IIA and IIB (NSGCT)?

1. Stage IIA—negative markers
    a. Primary NS-RPLND
    b. Primary chemotherapy: EP × 4 cycles or BEP × 3 cycles
2. Stage IIA—markers persistently elevated (S2)
    a. Primary chemotherapy: BEP × 4 cycles
3. Stage IIB—negative markers
    a. LN metastases within lymphatic drainage site (landing zone)
        i. Primary chemotherapy: EP × 4 cycles or BEP × 3 cycles
        ii. Primary RPLND in highly selected cases
    b. Multifocal LN metastases outside lymphatic drainage site (landing zone)
        i. Primary chemotherapy: EP × 4 cycles or BEP × 3 cycles
4. Stage IIB—markers persistently elevated (S2/S3)
    a. Primary chemotherapy: BEP × 4 cycles

What is growing teratoma syndrome?

Retroperitoneal masses that contain teratomas enlarge (sometimes rather quickly) in the face of normal tumor markers. Although these lesions are benign, they still warrant surgical excision. If left alone, teratomas may spread and often compromise vital organ function (e.g., bowel, ureters, vessels) by local invasion.

CASE 5

HPI: 25-year-old Caucasian male with testicular pain × 2 weeks plus scrotal swelling and pain; bilateral breast tenderness of new onset. No urinary complaints.

PMH: none

PSH: none

Allergies: none **Medications:** none

FH: (-) urologic cancer
SH: (-) tob; (-) ETOH
ROS: non-contributory

PE:

Vitals	T 98.6	BP 140/60	P 90	RR 12
GA	WDWN CM INAD			
HEENT	supraclavicular lymphadenopathy otherwise benign			
Heart	RRR			
Lungs	CTA			
Breasts	bilateral enlargement with palpable tenderness			
Abdomen	soft; NT/ND			
Flank	(-) CVAT			
GU	normal circumcised phallus; adequate meatus; (R) hemiscrotum firm and enlarged; (L) testicle WNL			
Prostate	smooth and benign @ 30 g; (-) nodules or induration			
Ext	(-) CCE			
Neuro	non-focal			

What initial lab tests do you order?

UA → WNL
CBC → WNL
Chem 7 → WNL

What is your differential diagnosis?

This patient has testicular tumor until proven otherwise. State that you would obtain scrotal ultrasound.

Scrotal US: (R) testis heterogeneous echogenicity; (L) testis normal

What is your assessment?

Testis tumor

What is your next step?

State that you would obtain tumor markers.

LDH:	600 U/L	
AFP:	1800 ng/mL	(0–10.0 ng/mL)
bhCG:	280 mIU/mL	(0–3.5 mIU/mL)
PLAP:	normal	(122–236 U/L)

What is your recommendation?

Recommend radical orchiectomy via inguinal approach.
Obtain preop consent.
Discuss and recommend sperm banking.
Give preop IV antibiotics.

What is the most likely pathology?

Non-seminomatous germ cell tumor.

Only NSGCT would cause elevation in AFP. Seminoma does not cause a rise in AFP.

Why does this patient have gynecomastia?

NSGCT is producing elevated levels of estradiol to cause gynecomastia.
Leydig cell tumor could produce gynecomastia by peripheral conversion of testosterone to estrogen but will not cause elevation in tumor markers.

What is your follow-up?

Ask for pathology report. Better to state that you would review the pathology specimen with the pathologist. In addition, obtain follow-up tumor markers.

Pathology: dense fibrotic scar; no active malignancy was present

LDH:	normal	
AFP:	300 ng/mL	(0–10.0 ng/mL)
bhCG:	20 mIU/mL	(0–3.5 mIU/mL)

What is your assessment?

He may have primary “burned-out” testis tumor or extragonadal tumor.

What is your recommendation?

He needs excisional biopsy or FNA of supraclavicular node. He agrees to proceed.

He underwent open biopsy of the node uneventfully.

What is your next step?

Check pathology report and review the slides.

Pathology: yolk sac, embryonal, and choriocarcinoma

What do you do now?

State that you would obtain additional staging work-up with CT scan of abdomen and pelvis, CXR, and liver function tests. Obtain bone scan if alk phos is elevated or if he is having bone pain.

Chest CT: multiple 2 cm lung nodules
Abd CT: 8 cm interaortocaval node; no other adenopathy or metastasis
Pelvic CT: normal
LFTs: normal
Alk phos: normal

What are the basic principles of testicular tumor markers?

1. Always obtain baseline pre-orchiectomy levels
2. Always obtain pre-chemotherapy and pre-radiotherapy levels
3. Always follow decay curve/half-life to monitor treatment response (it takes more than 5 half-lives to eliminate circulating markers—bhCG wait 2 weeks, AFP wait 5 weeks, LDH wait 3 weeks)
4. S stage is based upon nadir values of post-orchiectomy markers
5. Always follow decay curve to predict clinical course
6. Normal levels do not exclude presence of distant metastasis
7. Normalization during therapy does not imply tumor-free state. Do not stop treatment prematurely
8. Elevated markers imply persistence of tumor, and further therapy is warranted
9. Persistently elevated tumor markers mean that excision or exploration of a post-chemotherapy residual mass should not be undertaken. Further chemotherapy should be given instead
10. Slower than the expected rate of fall in markers implies a poor response to therapy
11. Transient "release phenomenon" with a sudden surge in markers within a few days of therapy should not be a cause for alarm

What is his clinical stage and prognosis?

Clinical stage III NSGCT. His 5-year survival rate is 90% with appropriate therapy.

What is his risk category?

The patient is in the "good risk" category.

Features that determine risk for nonseminoma are (poor versus good risk):

1. Mediastinal versus testicular/retroperitoneal primary
2. Non-pulmonary versus no non-pulmonary visceral metastases
3. Level of markers

What do you recommend?

Chemotherapy.

BEP × 4 cycles.

What is your next step?

Re-image chest and abdomen with CT scan.

Chest CT:	resolution of pulmonary mets
Abd CT:	reduction of interaortocaval node to 4 cm

What is your next step?

Repeat tumor markers.

LDH:	normal
AFP:	normal
bhCG:	normal

What do you recommend now?

Post-chemotherapy RPLND.

How do you proceed?

Obtain informed consent. Obtain preoperative labs. Bowel prep the patient with mechanical and antibiotic bowel prep. T&C 2 units. Give preop antibiotics and SCD.

Remember that he has received chemotherapy. Use room air FIO2 and be judicious with fluids. Discuss with anesthesiology preoperatively about the need for low inspired oxygen level and low crystalloid replacement during the perioperative period.

Describe the procedure:

Patients with significant retroperitoneal tumor involvement are best approached via thoracoabdominal incision. However, transabdominal approach may be used in patients with minimal disease such as this patient.

The Operation (Post-chemo RPLND)

During the operation, the mass is stuck to the vena cava, and you cannot dissect it out.

What do you do?

Resect the mass and part of the vena cava.
If the entire vena cava needs to be resected, use pericardial patch or PTFE (prosthetic) graft to reconstruct the cava.

During the operation, the mass is enveloping the right kidney, and you cannot dissect it out.

What do you do now?

Resect the mass and perform nephrectomy (occurs in ~10% PC-RPLND).

You finally remove the entire mass and complete the RPLND.

The final pathology is fibrosis only.

What is your follow-up?

1. CXR and tumor markers Q 3 months × 2 years, then Q 6 months × 3 years
2. CT scan (abdomen and pelvis) Q 6 months

NCCN Guidelines—Clinical stage II-III, NSGCT: Surveillance After Complete Response to Chemo ± Post-chemo RPLND*

HPI and tumor markers
    Year 1: q 2 mo
        2: q 3 mo
        3–5: q 6 mo
Abdominal/Pelvic CT
    Year 1: q 6 mo
        2: 1 × / yr
        3–5: Not indicated
Chest X-ray
    Year 1–2: q 6 mo
        3–4: 1 × / yr
        5: Not indicated

*Adapted from: NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Testicular Cancer Version 2.2017. © 2016 National Comprehensive Cancer Network, Inc.

1 year later his bhCG is elevated at 50 mIU/mL.

What do you recommend now?

Give testosterone injection and re-measure bhCG.

His bhCG may be falsely elevated due to the fact he only has a single testicle. Loss of a testicle may result in low testosterone level.

Low testosterone will stimulate anterior pituitary to increase production of LH. LH has cross-reactivity with bhCG and will cause false elevation of bhCG.

If bhCG returns to normal after testosterone injection, no further action needs to be taken.

CHAPTER 8

INFECTIOUS DISEASES

JEREMY BERGAMO, MD
LAWRENCE YEUNG, MD

CASE 1

HPI: 45-year-old Caucasian male with history of HIV and IDDM is referred from an outside hospital after presenting with left side flank pain, fever, dysuria, and occasional hematuria. Workup revealed a 3 cm left renal pelvis stone with hydronephrosis. Attempt at stent placement was unsuccessful, thus a nephrostomy tube was placed. He denies a history of stones or previous GU surgery. He presents to you now for further management.

PMH: IDDM; HIV

PSH: RIH repair; cystoscopy; retrograde pyelogram; failed attempt at stent placement

Allergies: none **Medications:** Ampicillin; Gentamicin, Insulin; HAART therapy

FH: non-contributory
SH: (-) tob; (+) social ETOH
ROS: non-contributory

PE:

Vitals	T 101.3 BP 154/78 P 102 RR 12
GA	cachectic appearing CM in mild distress
HEENT	unremarkable
Heart	RRR
Lungs	CTA B
Abdomen	soft; non-tender non-distended; no masses
Flank	mild (L) CVA tenderness; nephrostomy tube draining cloudy urine
GU	normal circumcised phallus; adequate meatus; bilateral testicles WNL
Prostate	30 g; smooth and benign
Ext	no cyanosis, clubbing, or edema
Neuro	non-focal

Labs:

Note: Remember to send off fungal culture.

CBC: → WBC 16 K/μL; Hgb 13 g/dL; HCT 36%
Chem 7: → Na 140 meq/L; K 4.0 meq/L; Cl 100 meq/L; CO 24 meq/L; glucose 220mg/dL; BUN 10 mg/dL; Cr 1.3 mg/dL
UA: → many WBC; 5–6 RBC/HPF; + hyphae; pH 6.0
Urine Cx: → positive Candida albicans
Fungal Cx: → positive Candida albicans
Blood Cx: → positive Candida albicans

What initial imaging studies would you obtain?

CT-IVP to evaluate microscopic hematuria and stone burden.

CT-IVP: 3.0 cm × 1.8 cm radiopaque calculus (700 HU) within (L) renal pelvis; (L) lower pole, non-enhancing mass; no obstruction; contrast courses down distally to the urinary bladder

What is your differential diagnosis of the filling defect?

Fungus ball, blood clot, radiolucent calculus, sloughed papilla.

What is your assessment?

45-year-old CM with (L) renal calculus and left lower pole filling defect.
Patient also with funguria and fungemia.

How would you proceed?

You start patient on anti-fungal such as Fluconazole.

After 72 hours, patient becomes afebrile with normal vital signs.

How do you address the filling defect?

You decide to take him to the operating room for diagnostic ureteroscopy to evaluate the left lower pole filling defect. During the procedure, you note a large amount of white, cloudy urine in the bladder. This is sent for cultures.

Left ureteroscopy is performed and a 3 cm renal pelvis stone is encountered along with a large left lower pole fungal ball. The stone is not treated ureteroscopically because of the size of the stone as well as the present funguria.

What is your diagnosis and how would you treat this?

Patient has renal and bladder candidiasis.

Renal candidiasis should be treated with intravenous amphotericin B.

Can perform renal/bladder anti-fungal irrigant via nephrostomy tube or Foley catheter with:

1. Fluconazole
2. Additionally, Amphotericin B can be administered (50 mg in 1 L sterile water over 24 hours). Can repeat for up to a week

Repeat urine culture. Obtain a renal US to assess resolution of fungus ball.

What are some side effects of Amphotericin B?

Chills, rigor, fevers, phlebitis, bone marrow toxicity, and potassium and magnesium depletion. Be sure to check electrolytes while on amphotericin B.

You place the patient in IV Amphotericin B and perform Amphotericin B renal irrigation via the nephrostomy tube. At end of 7 days, urine culture and renal ultrasound revealed no evidence of remaining fungal ball.

What is your next step if the fungal ball persists?

Consider debulking the fungus ball percutaneously.

What is your next step for this patient?

Proceed with PCNL for the remaining calculus.

How would you prepare this patient?

1. Obtain informed consent
2. Discuss the surgical procedure, indications, potential risks and complications

3. State you would get appropriate preoperative work up: CXR, EKG, and labs—especially PT, PTT, and platelets. Repeat urine culture. Give prophylactic intravenous antibiotics preoperatively

What are the AUA Antimicrobial Prophylaxis Best Practice Recommendations for PCNL?

Procedure	Organisms	Prophylaxis indicated	Antimicrobials of Choice	Alternatives	Duration of Therapy
PCNL	GU-tract and skin	In all patients	1st/2nd generation Cephalosporin (e.g., Cefazolin, Cefotetan) Aminoglycoside + Metronidazole or Clindamycin	Ampicillin/ Sulbactam Fluoroquinolone	24 hours

Note: Urine culture must be negative prior to treatment.

Source: Wolf JS Jr., Bennett CJ, Dmochowski RR, et al. Best Practice Policy Statement on Urologic Surgery Antimicrobial Prophylaxis. J Urol 2008;179:1379–90 Table 3a. Copyright© 2008 American Urological Association. Published by Elsevier Inc. Used with permission. (https://www.auanet.org/education/guidelines/antimicrobial-prophylaxis.cfm)

What is your surgical technique for a PCNL?

1. Insert a Foley catheter, and then place the patient in a prone position
2. Be sure to pad all pressure points, place 2 guide wires (e.g., safety wire and working wire) through the perc tube
3. Dilate the tract under fluoroscopy
4. Remove all stone fragments
5. Insert a nephrostomy tube (i.e., Foley catheter), and perform nephrostogram to rule out injury to renal pelvis or ureter
6. Follow up stone composition

What are the intraoperative complications and management?

1. Venous bleeding—Stop the operation and place and inflate a Foley catheter in the renal pelvis to tamponade the bleeding
2. Arterial bleeding—Stop the operation and do arteriogram and embolize vessel
3. Stone migrated out of the renal pelvis—Stop the operation and leave stone
4. Significant tear in the renal pelvis—Stop the operation
5. Irrigation mismatch—Stop the operation if irrigant loss is more than 1000 mL

What is your post-operative management?

Immediately post-op, obtain a non-contrast CT scan to evaluate for residual calculus, post-op hematoma, and pneumothorax (risk due to upper pole access), and/or perinephric fluid accumulation. Use bone windows to help distinguish stone from nephrostomy tube/stent.

Obtain an antegrade nephrostogram if urine is clear on POD #1 or 2, clamp and remove the nephrostomy tube if there is no evidence of extravasation. Obtain follow-up imaging (i.e., CTIVP) at 6–12 weeks to document complete stone clearance/absence of obstruction. Follow-up on stone composition.

CASE 2

HPI: 55-year-old Caucasian male with a history of HIV, HTN, and BPH status post TRUS biopsy 2 days ago for elevated PSA of 5.7 ng/mL presents now with fever, chills, nausea, and vomiting. He denies hematuria or rectal bleeding. He states he has been able to void but has difficulty emptying his bladder completely and reports dribbling. He did not receive pre- or post-procedure antibiotics.

PMH: HIV, HTN, BPH

PSH: cholecystectomy

Allergies: none **Medications:** Captopril

SH: (-) tob; (-) ETOH use
FH: positive CAP
ROS: non-contributory

PE:

Vitals	T 103.3 BP 90/50 P 120 RR 14
GA	well-nourished, well-developed CM in moderate distress
HEENT	unremarkable
Heart	RRR
Lungs	CTA B
Abdomen	soft, moderate suprapubic fullness with tenderness
Flank	no CVAT
GU	normal circumcised phallus; adequate meatus; testicles WNL bilaterally
Prostate	warm, enlarged, fluctuant
Ext	no cyanosis, clubbing, or edema
Neuro	non-focal

Note: Must do a gentle prostate examination carefully. Do not massage the prostate as it may promote/worsen sepsis.

Labs:

CBC:	→	WBC 22 K/μL; Hgb 13 g/dL; HCT 36%
Chem 7:	→	Na 140 meq/L; K 4.0 meq/L; Cl 100 meq/L; CO_2 24 meq/L; glucose 220 mg/dL; BUN 10 mg/dL; Cr 1.3 mg/dL
UA:	→	many WBC; 5–6 RBC/HPF; TNTC bacteria
Urine Cx:	→	> 100,000 colonies of E. coli (pansensitive)
Fungal Cx:	→	pending
Blood Cx:	→	pending

What is your assessment?

55-year-old CM with acute prostatitis and possible urinary retention.

What are the AUA Antimicrobial Prophylaxis Best Practice Recommendations for TRUS biopsy?

Procedure	Organisms	Prophylaxis Indicated	Antimicrobial of Choice	Alternative Choice	Duration of Therapy
Transrectal prostate biopsy	Intestine	All patients	Fluoroquinolone 1st/2nd/3rd gen Cephalosporin	TMP-SMX Aminoglycoside	24 hours

Source: Wolf JS Jr., Bennett CJ, Dmochowski RR, et al. Best Practice Policy Statement on Urologic Surgery Antimicrobial Prophylaxis. J Urol 2008;179:1379–90 Table 3a. Copyright© 2008 American Urological Association. Published by Elsevier Inc. Used with permission. (https://www.auanet.org/education/guidelines/antimicrobial-prophylaxis.cfm)

What is your initial step?

You begin IVF and order IV antibiotics (e.g., Ceftriaxone or Ciprofloxacin). 2 hours later he is hemodynamically stable. However, he continues to complain of suprapubic fullness and tenderness.

What is your next step?

Obtain PVR using bladder ultrasound. If PVR is elevated, place a suprapubic tube (SPT).

PVR obtained: 1100 mL

Describe how you would place SPT.

1. Obtain informed consent
2. Palpate 2 finger breadths above pubic symphysis in the midline and anesthetize skin and intended SP tract
3. Identify bladder by aspiration with spinal needle and place SPT using kit that incorporates Seldinger technique over guidewire

   Note: While many other techniques are available, you should consider the safest technique possible for purposes of the oral exam.

4. If examiner gives scenario of hostile abdomen, have SPT placed under imaging guidance by interventional radiology

SPT placed with return of 1100 mL cloudy urine.

Why is placing a Foley catheter contraindicated in this situation?

Foley catheter may exacerbate his prostatitis.

What would you do next?

Admit the patient to the hospital. Continue intravenous antibiotics and monitor him.

After 2 days of intravenous antibiotics, he remains febrile and has persistent leukocytosis.

What is your differential diagnosis?

Acute prostatitis versus prostatic abscess.

What imaging studies would you obtain?

CT scan (±) contrast.

Report: 3 cm low attenuation lesion within the prostate; normal kidneys; no kidney or ureteral stones

What would you do next?

This patient has a prostatic abscess that must be decompressed. The treatment options include the following:

1. Transrectal or transperineal ultrasound-guided needle aspiration
2. Transurethral unroofing of the abscess

How do you proceed?

Patient elects TUR of prostate abscess.

Obtain informed consent, order preoperative labs, and continue IV antibiotics.

During the resection, a purulent material exudes from the prostate that you have unroofed.

Note: Make sure to send culture for aerobic bacteria, anaerobic bacteria, mycobacteria, and fungus.

Aerobic Cx: → E. coli (pansensitive)
Anaerobic Cx: → no growth
Fungal Cx: → no growth
Blood Cx: → no growth

What do you do now?

Follow-up on his leukocytosis to ensure that it resolves. WBC now 10.

What is your follow-up?

You discharge him home with a 4-week course of TMP-SMX.

You follow up on the prostate TUR specimen, which result shows BPH and no malignancy.

He undergoes a voiding trial in the clinic and has a PVR of 20 mL, and you remove the SPT.

What are the common and rare side effects associated with TMP-SMX?

1. Common
    a. GI upset (nausea, vomiting)
    b. Skin reactions (rash, urticaria)
2. Rare
    a. Stevens-Johnson syndrome
    b. Toxic epidermal necrolysis
    c. Fulminant hepatic necrosis
    d. Blood dyscrasias such as aplastic anemia, agranulocytosis
    e. Angioedema

CASE 3

HPI: 55-year-old African-American male with history of diabetes presents with fever, malaise, and scrotal pain for the past 5 days. He denies nausea or vomiting, but reports extreme fatigue and lethargy recently. He denies any symptoms of UTI including dysuria, hematuria, frequency, or urgency. He does complain of a painful boil on his R hemiscrotum that has been intermittently draining for the past few days. He denies any history of stones. He does not have HIV or history of IV drug abuse.

PMH: IDDM

PSH: appendectomy, tonsillectomy

Allergies: PCN **Medications:** Insulin 20 units SQ BID

FH: none
SH: (-) tob; (+) ETOH use, occasional
ROS: non-contributory

PE:

Vitals	T 102.3	BP 90/40	P 110	RR 18
GA	lethargic, ill appearing AAM			
HEENT	unremarkable			
Heart	RRR			
Lungs	CTA B			
Abdomen	soft; non-tender; non-distended; no masses			
Flank	no CVAT			
GU	normal circumcised phallus; adequate meatus; bilateral testicles WNL; black necrotic area (3 cm) with surrounding erythema and tenderness around the scrotum and perineum; positive crepitus in the perineal area			
Prostate	30 g; smooth and benign			
Rectal	no perirectal abscess			
Extremities	no clubbing, cyanosis, or edema			
Neuro	non-focal			

What is your assessment?

His genital examination is highly suspicious for genital (Fournier's) gangrene. Presence of crepitus indicates there is gas in the underlying subcutaneous tissues.

Labs:

CBC: → WBC 23 K/µL; Hgb 13 g/dL; HCT 36%
Chem 7: → Na 142 meq/L; K 3.8 meq/L; Cl 100 meq/L; CO_2 18 meq/L; glucose 300 mg/dL; BUN 50 mg/dL; Cr 1.8 mg/dL
UA: → normal
Urine Cx: → no growth
HIV: → non-reactive

Blood Cx:	→	negative
Gram stain:	→	gram (+) and gram (-) organisms
Wound Cx:	→	multiple aerobic and anaerobic organisms

What would you do first?

You must stabilize the septic patient. Begin IV antibiotics and stabilize the patient with IVF after sending off appropriate cultures. Begin triple antibiotic coverage with Vancomycin (since patient is PCN allergic), Gentamicin, and Metronidazole or Clindamycin.

What imaging studies can you obtain?

CT pelvis with and without contrast: positive subcutaneous gas overlying the perineal and scrotal region.

What clinical conditions is genital (Fournier's) gangrene most often associated with?

Fournier's gangrene is often associated with urethral stricture and/or perirectal abscess.

What studies can be done to evaluate for source of infection?

Perform retrograde urethrogram and cystoscopy to evaluate for urethral stricture, as well as obtain general surgery consult if there is concern for peri-rectal abscess.

Retrograde urethrogram:	no stricture or extravasation
Cystoscopy:	normal
Proctoscopy:	normal

Note: Genital (Fournier's) gangrene is a life-threatening urological emergency. The diagnosis is made clinically, i.e., based on history and physical exam. Although special studies may be performed, they should not delay emergent surgical debridement of all necrotic tissue.

What would you do next?

Surgical debridement.

Obtain the appropriate preoperative labs including CXR, EKG, PT/PTT, T&C, an informed consent, and take the patient to the operating room for aggressive surgical debridement.

During the informed consent, you must discuss possibility of SPT and/or diverting colostomy. Be able to discuss intraoperative technique.

Note: Watchful waiting with intravenous antibiotic therapy is not an acceptable answer. Simple incision and drainage of the scrotal abscess without intraoperative surgical debridement is also an unacceptable answer.

What do you think will happen if you performed simple incision and drainage?

The erythema and crepitus will march up the anterior abdominal wall along Scarpa's fascia to the clavicles.

What is your surgical technique for perineal debridement for Fournier's Gangrene?

1. Place the patient in dorsal lithotomy position
2. Wide debridement of necrotic tissue to healthy bleeding tissue
3. Send an intraoperative Gram stain and fluid/tissue culture and sensitivity
4. Consider SPT to divert urine to facilitate wound care
5. Have general surgeon perform diverting colostomy if debridement nears rectum and wound care may be compromised by fecal contamination
6. Pack the wound

How would you manage this patient postoperatively?

1. Wet to dry dressing changes
2. Re-evaluation of the wound and continued debridement as necessary
3. Continue IV antibiotics and follow-up on cultures
4. Obtain a plastic surgery consult for future perineal skin coverage, or perform yourself with split thickness skin graft

CASE 4

HPI: 48-year-old Asian female presents with a 5–6 month history of intermittent urinary frequency, urgency, and dysuria. She reports voiding every 2–3 hours during the day and waking up 4 times each night. She also reports a burning sensation while voiding as well as urgency without incontinence. She denies hematuria, nausea, vomiting, or diarrhea. She does not have diabetes or any history of stone disease. Her last menstrual cycle is unknown and she underwent TAH/BSO 6 months ago for endometriosis. She immigrated from Japan 5 years ago.

PMH: endometriosis

PSH: laparoscopy; bilateral tubal ligation; TAH/BSO for endometriosis

Allergies: none **Medications:** none

FH: none
SH: (+) tob, 20 pack year; (-) ETOH; works as a housewife
ROS: non-contributory

PE:

Vitals	T 98.3	BP 140/60	P 90	RR 18
GA	well developed, well-nourished AF in no acute distress			
HEENT	unremarkable			
Heart	RRR			
Lungs	CTA B			
Abdomen	soft; non-tender non-distended; no masses			
Flank	no CVA tenderness			
Pelvic	normal female			
Rectal	benign			
Ext	no clubbing, cyanosis, or edema			
Neuro	non-focal			

Labs:

UA:	→	10–15 RBCs/HPF; 20–30 WBCs/HPF; no bacteria
Urine Cx:	→	no growth
CBC:	→	WBC 9 K/μL; Hgb 13 g/dL; HCT 36%
Chem 7:	→	Na 135 meq/L; K 4.2 meq/L; Cl 100 meq/L; CO2 24 meq/L; glucose 100 mg/dL; BUN 12 mg/dL; Cr 1.0 mg/dL

What is your differential diagnosis?

This patient has **sterile pyuria** and microscopic hematuria. The differential diagnosis includes tuberculosis, bladder tumor (CIS), overactive bladder, and interstitial cystitis.

What would you do first?

1. Send off urine cytology and order CT-IVP and cystoscopy to evaluate microscopic hematuria in this patient with risk factors for transitional cell carcinoma (smoking history)
2. In addition, place a PPD, and send off fresh voided morning urine for AFB stain and TB culture

3. Also check her ESR, obtain a CXR, and check LFTs in case you have to begin anti-TB medications

Urine cytology: positive inflammatory cells; no malignant cells

CT-IVP:	5 mm (R) distal ureteric stricture associated with moderate hydronephrosis; cortex appears thick; (L) kidney and collecting system normal
Cystoscopy:	cobblestone mucosa around (R) ureteral orifice; no tumors or CIS; bladder is trabeculated
PPD:	positive skin test
AFB stain:	positive tuberculosis bacilli; "red snappers"
Urine Cx:	few Mycobacteria growing
ESR:	80 mm/hr; normal: (0–30 mm/hr)
LFTs:	normal
CXR:	apical scarring

Do you want to obtain any special studies?

State you would perform cystoscopy under anesthesia and obtain bladder biopsies.
In addition, you perform a (R) retrograde pyelogram with (R) ureteral washing, and place a (R) stent.

Ureteroscopy:	no lesion within the ureter
Cystoscopy:	cobblestone appearance around the (R) ureteral orifice; extremely trabeculated and contracted urinary bladder
Bladder wash:	negative for malignancy
Ureteral wash:	negative for malignancy
Retrograde pyelogram:	5 mm stricture of distal ureter; contrast courses up the ureter and into renal pelvis
Bladder biopsy:	granulomatous cystitis

After you did the retrograde pyelogram, you passed the ureteral catheter past the stricture and obtained urine. You sent the urine off for aerobic, anaerobic, fungal, and TB cultures. This urine culture grows Mycobacterium tuberculosis.

What is your assessment?

She has urinary tuberculosis with ureteral obstruction.

What are your treatment options?

1. Watchful waiting
   a. Not a good choice. If you pursue this course, she will have continued voiding symptoms
   b. She will also develop a longer stricture at the (R) UVJ with worsening hydronephrosis, and azotemia
   c. At this point you must begin anti-TB medication
2. Bacterial antibiotics
   a. This patient has urinary tuberculosis, not typical bacterial cystitis. This is the wrong protocol
   b. Routine antibiotics will not solve this problem. Previous bacterial antibiotics have not worked, and therefore repeat antibiotics will not work
3. Begin anticholinergics

   a. This patient does not have overactive bladder. Although she has urinary frequency and urgency symptoms, her problem is most consistent with urinary tuberculosis rather than overactive bladder
   b. Anticholinergics will help her voiding symptoms but they will not treat her tuberculosis
4. Treat for interstitial cystitis (IC)
   a. This patient does not have IC. However, if you follow this protocol, you need to discuss how you would treat IC
   b. After treatment, she will continue to have bladder symptoms and follow-up IVP will show longer stricture at the (R) UVJ. At this point you must begin anti-tuberculous medication
5. Anti-tuberculous drug therapy
   a. This is the best initial therapy
   b. The first therapeutic procedure involves beginning anti-tuberculous medications as soon as possible
      i. INH, Rifampin, Ethambutol, and Pyrazinamide are given daily for the first 2 months, and then INH and Rifampin are given 3 times per week for an additional 2 months
      ii. When this protocol is chosen, you must follow-up with urine culture for TB and sensitivity. In addition, obtain CT-IVP 3–6 months later

      Note: You must check LFTs and caution the patient not to drink alcohol while on these anti-tuberculosis medications.
6. Ureteral reimplantation
   a. This is a bad recommendation as an initial therapy because this protocol is too aggressive
   b. In addition, you did not consider less invasive treatment such as balloon dilation
   c. Your examiner could fail you on this question since you did not diagnose urinary tuberculosis and proceeded to reimplant the ureter

What is your follow-up?

Follow-up with urine culture for TB and sensitivity. In addition, obtain IVP at 3 months and 6 months later.

Urine Cx for TB: no growth

3 months later, she returns to your clinic for repeat CT-IVP.

CT-IVP: (R) UVJ stricture has progressed now to a 1 cm stricture

What would you do next?

1. Give Prednisone 20 mg po QD × 4–6 weeks. This is the initial treatment of choice for tuberculous ureteritis that can lead to stricture formation
2. If Prednisone does not work, then balloon dilation should be considered. Balloon dilation/laser incision/stent placement is not the initial treatment of choice

She fails Prednisone, so you proceed with ureteral balloon dilation, which the stricture responds to nicely. She returns to your clinic a year later complaining of recurrent voiding symptoms and new incontinence.

How do you proceed?

State that you will obtain a detailed history and perform a thorough physical examination.

She reports still having frequency every 2 hours, with an increase in nocturia 5×/night as well as continued burning sensation during voids. She denies hematuria or stress incontinence but reports incontinence associated with urgency. She reports taking her anti-TB medications as prescribed with no side effects.

PE:

Vitals	T 98.3	BP 140/60	P 90	RR 18
General appearance	well developed, well nourished, AF in no acute distress			
Abdomen	soft, non-tender, non-distended; no masses			
Flank	no CVA tenderness			
Pelvic	normal F			

Labs:

CBC → normal
Chem 7 → WNL; Cr 1.2 mg/dL
UA → negative
UCx → no growth
UCx for TB → no growth

What is your assessment?

Remember that she had a contracted bladder during previous cystoscopy. She needs urodynamics now.

Note: You must not forget the bladder. She had small capacity bladder due to chronic inflammation from tuberculosis.

Results of video-urodynamics:

Noninvasive urodynamics:		
Qmax	30 cc/s	
Voided volume	150 mL	
PVR	5 cc	
Filling CMG:		
Bladder capacity	150 mL	
Compliance	6 cc/cm H_2O	(poorly compliant)
DLPP	50 cm H_2O	(normal < 40 cm H_2O)
ALPP	no stress incontinence	
VUCG	small capacity bladder; grade I/V VUR on left	
Pressure-flow:		
Pdet Qmax	10 cm H_2O	(normal)
Qmax	28 cc/s	(normal)
Voided volume	150 mL	(normal)
PVR:	10 mL	(normal)
Flow pattern:	bell-shaped; (-) abdominal straining	
Electromyogram (EMG):	negative for detrusor sphincter dyssynergia	

What is your assessment?

She has poorly compliant, small capacity bladder and high detrusor leak point pressure.

What are your treatment options?

1. Anticholinergic therapy—this is a reasonable initial treatment. Although if this fails, you must discuss surgical options (see below)
2. Sacral neuromodulation—this is a reasonable alternative prior to definitive surgery if pharmacotherapy fails; however, this is not the correct initial treatment
3. Augmentation cystoplasty—urinary bladder may be augmented using Snow procedure (autoaugmentation) or using a segment of bowel (enterocystoplasty). Patient must be willing to catheterize self. Be prepared to discuss your operation

What is your surgical technique for an autoaugmentation procedure?

1. Dissect the detrusor muscle off the bladder mucosa
2. Affix the detrusor wings to the psoas muscle. Be sure not to injure the genitofemoral nerve. This essentially creates a large bladder diverticulum
3. If bladder mucosa sustains holes during dissection, repair with absorbable sutures
4. Place a drain and Foley catheter

What is your surgical technique for an enterocystoplasty procedure?

1. Bivalve the bladder at dome
2. Harvest a 25–30 segment of ileum at least 15 cm proximal to ileocecal valve
3. Open the antimesenteric border and fold posterior wall back on itself and sew together using 2-0 absorbable suture
4. Attach the ileal patch to the dome of bladder at cystotomy site
5. Place SPT, drain, and Foley catheter

Note: The risk of augmentation cystoplasty is possible urinary retention. You need to discuss the need for CIC postoperatively with your patient. If she does not wish to catheterize her urethra, you need to discuss a continent diversion.

Continent diversion using Mitrofanoff principle—if the patient does not wish to catheterize via urethra and does not wish to wear a bag, this is a reasonable alternative.

Cystectomy and ileal loop would be a final option based on patient preference or if above surgeries cannot be performed.

CASE 5

HPI: 33-year-old C5 injury quadriplegic Caucasian male who has been experiencing fever, chills, nausea, and vomiting for the past 48 hours. He has also noticed cloudy urine from his SPT tube for the past week. He denies any hematuria. He reports a history of stone disease in the past but is unable to recall details. He is not currently on any suppressive antibiotics and has not received imaging studies for many years.

PMH: C5 quadriplegic

PSH: SPT placement

Allergies: none **Medications:** none

FH: (-) history of nephrolithiasis
SH: (-) tob; (-) ETOH
ROS: non-contributory

PE:

Vitals	T 102.6	BP 100/64	P 120	RR 20
GA	toxic appearing young CM sitting in a wheelchair			
HEENT	unremarkable			
Heart	RRR			
Lungs	CTA B			
Abdomen	soft; non-tender, non-distended; SPT in place draining cloudy urine			
Flank	positive (R) CVA tenderness			
GU	normal phallus; testicles WNL bilaterally			
Prostate	smooth and benign			
Extremities	contracted			
Neuro	consistent with C5 neurological lesion			

Labs:

UA:	→	pH 8; 4–12 RBC/HPF; 10–20 WBC/HPF; (+) nitrites; (+) leukocyte esterase
Urine Cx:	→	pending
CBC:	→	WBC 16 K/µL; Hgb 13 g/dL; Hct 39%
Chem 7	→	WNL; Cr 1.3 mg/dL
Blood Cx:	→	pending

What are the AUA Antimicrobial Prophylaxis Best Practice Recommendations for removal of an external urinary catheter?

Prophylaxis indicated only if the patient has risk factors including: advanced age, anatomic anomaly of the urinary tract, poor nutritional status, smoking, chronic corticosteroid use, immunodeficiency, co-occurring infection, and/or prolonged hospitalization.

Procedure	Organisms	Prophylaxis Indicated	Antimicrobial of Choice	Alternative Antimicrobials	Duration of therapy
Removal of external urinary catheter	GU tract	If risk factors	Fluoroquinolone TMP-SMX	Aminoglycoside with or without Ampicillin 1st or 2nd generation Cephalosporin Amoxicillin/Clavulanate	24 hours

Source: Wolf JS Jr., Bennett CJ, Dmochowski RR, et al. Best Practice Policy Statement on Urologic Surgery Antimicrobial Prophylaxis. J Urol 2008;179:1379–90 Table 3a. Copyright© 2008 American Urological Association. Published by Elsevier Inc. Used with permission. (https://www.auanet.org/education/guidelines/antimicrobial-prophylaxis.cfm)

What would you do first?

1. State that you would stabilize him first and treat his UTI
2. Admit to the hospital and start IVF
3. Send blood and urine cultures and then start broad spectrum IV antibiotics
4. Ensure he is hemodynamically stable

What is your next step?

Obtain CT-IVP (to evaluate for microscopic hematuria and infectious etiology) and follow up on culture results.

CT scan	7 cm branched staghorn calculus in (R) kidney without hydronephrosis; severely atrophic (L) kidney; (L) hydronephrosis and (L) perinephric abscess with 9 mm left proximal ureteral stone
Culture results:	Urine culture: > 100,000 colonies of Proteus mirabilis (pan-sensitive) Blood cultures: positive for gram negative rods

What is your assessment?

33-year-old CM with (R) staghorn calculus and (L) perinephric abscess with Proteus mirabilis UTI and microscopic hematuria.

What is your next step?

Adjust antibiotic coverage based on culture results.

What is your first step in managing perinephric abscess?

Send patient to interventional radiology to place percutaneous drain in the (L) perinephric abscess and place a (L) nephrostomy tube to decompress the obstructed kidney.
Send aerobic, anaerobic and fungal cultures of the abscess fluid.

After 24 hours, he stabilizes and is afebrile. Remove the percutaneous abscess drain when output is minimal.

What is your next step in evaluation?

Note: Need to assess renal function of (L) kidney after a period of decompression.

You ordered a MAG-3 renal scan to assess function of both kidneys 6 weeks after percutaneous renal drainage.

Results: MAG-3 scan → 93% function (R) kidney;
7% function (L) kidney

What is your assessment?

Severely atrophic, minimally functioning left kidney with obstructing 9 mm left proximal ureteral stone with history of perinephric abscess.

What is your recommendation?

Recommend a staged procedure starting with PCNL for (R) staghorn stone followed by asynchronous (L) simple nephrectomy.

In this scenario, you want to be as conservative as possible and remove the infectious source (right staghorn calculus) before proceeding to nephrectomy. Additionally, performing the nephrectomy second will allow the patient to make it through the PCNL with maximal nephrons and give time for the inflammation from the perinephric abscess to resolve.

Note: Need to complete hematuria work-up with cytology and cystoscopy.

Cytology	→	no malignant cells
Cystoscopy	→	inflammatory changes from chronic indwelling SPT

What is your next step?

1. Obtain informed consent for (R) PCNL
2. Discuss the surgical procedure, indications, potential risks and complications
3. Perform appropriate preoperative work up; CXR, EKG and labs—especially PT, PTT, and platelets. Send pre-operative urine culture. Give prophylactic antibiotics peri-operatively

What are the AUA Antimicrobial Prophylaxis Best Practice Recommendations for PCNL?

Procedure	Organisms	Prophylaxis Indicated	Antimicrobials of Choice	Alternatives	Duration of Therapy
PCNL	GU-tract and skin	In all patients	1st/2nd generation Cephalosporin (e.g., Cefazolin, Cefotetan) Aminoglycoside + Metronidazole or Clindamycin	Ampicillin/Sulbactam Fluoroquinolone	24 hours

Note: Urine culture must be negative prior to treatment.

Source: Wolf JS Jr., Bennett CJ, Dmochowski RR, et al. Best Practice Policy Statement on Urologic Surgery Antimicrobial Prophylaxis. J Urol 2008;179:1379–90 Table 3a.

Copyright© 2008 American Urological Association. Published by Elsevier Inc. Used with permission.
(https://www.auanet.org/education/guidelines/antimicrobial-prophylaxis.cfm)

Percutaneous access is obtained either by the interventional radiologist or you on the day of the operation. Upper pole calyx is accessed.

What is your surgical technique for PCNL?

1. Insert a Foley catheter, then place the patient in a prone position
2. Be sure to pad all pressure points, place 2 guide wires (e.g., safety wire and working wire) through the percutaneous tube
3. Dilate the tract under fluoroscopy
4. Remove all stone fragments
5. Insert a nephrostomy tube, and perform nephrostogram to rule out injury to renal pelvis or ureter
6. Obtain CXR in recovery room to rule out PTX due to upper pole access
7. Follow up stone composition

The patient does well from PCNL and returns to see you in 3 months in clinic.

What do you do now?

1. Reimage kidneys with non-contrast CT scan. This shows a normal appearing right kidney with no stones remaining and an atrophic left kidney with a left nephrostomy tube in place and completely resolved perinephric abscess. The 9 mm left proximal ureteral stone is still in place
2. Re-evaluate renal function: Cr 1.2

What do you do now?

Recommend (L) simple nephrectomy via extraperitoneal approach for minimally functioning kidney.

Note: Many other nephrectomy techniques are available to remove this kidney such as a laparoscopic simple nephrectomy. Whichever method you choose, be ready to explain your technique and any potential complications associated with it.

How do you proceed?

Get informed consent and preoperative labs. T&C 2 units blood.
Send pre-operative urine cultures from the bladder and (L) nephrostomy tube.
Give prophylactic antibiotics/culture directed antibiotics and place SCDs preoperatively.

What is your surgical technique for simple nephrectomy?

1. Start with an extraperitoneal flank incision over the kidney rest
2. Incise over 11th or 12th rib
3. Open Gerota's fascia and perinephric fat
4. Free up the entire kidney and identify the renal hilum
5. Dissect out nephrostomy tube tract and remove nephrostomy tube, taking care to minimize spillage of urine into field. Consider placing purse-string suture around nephrostomy tube prior to removal of tube to limit urine spillage

6. Ligate and divide renal artery, vein, and ureter

   Note: Because this patient has a 9 mm stone in the proximal ureter, should divide ureter as far distal as possible (i.e., at crossing of iliac vessels) to ensure removal of the stone. Should consider opening ureter on the back table once specimen has been removed to identify stone.

7. Finally, irrigate the wound, place a drain, and close the incision

He tolerates the operation well without complications.

What is your follow-up?

You need to check the pathology report.

Pathology: kidney with diffuse pyelonephritis and renal abscess; no malignancy.

CASE 6

HPI: 57-year-old Caucasian male is referred to you for a PSA of 4.3 ng/mL. He reports his PCP drew this 5 days ago for routine prostate cancer screening. This is his first PSA level, but he reports normal DREs in the past. He also reports some voiding symptoms for the past month including frequency 10×/day, nocturia 2–3×/night, and occasional dysuria described as burning. His AUA symptom score is 17. He denies hematuria, flank pain, constitutional symptoms, history of UTIs, STDs, or urethral discharge.

PMH: HTN

PSH: appendectomy at age 8 years

Allergies: none **Medications:** Lisinopril

FH: no FH of prostate cancer
SH: (-) tob; (+) ETOH, socially on occasion
ROS: non-contributory

PE:

Vitals	T 98	BP 120/70	P 64	RR 14
GA	well-developed, well-nourished CM in no acute distress			
HEENT	unremarkable			
Heart	RRR			
Lungs	CTA B			
Abdomen	soft; non-tender; non-distended			
Flank	no CVA tenderness			
GU	normal uncircumcised phallus; bilateral testicles WNL			
Prostate	45 g; tender to palpation; no nodule/fluctuance/induration			
Ext	no clubbing, cyanosis, or edema			
Neuro	non-focal			

Labs:

Chem 7 → WNL, Cr- 1.1
UA: → (-) blood and glucose; pH 5; RBC 1; WBC 5–10/HPF
UCx: → 10,000–50,000 E. coli (pansensitive)
EPS/ Post-massage UA: → > 100 WBC/HPF

What is your assessment?

The patient likely has chronic bacterial prostatitis.

What initial X-ray studies would you obtain?

None are indicated at this point. If you suspected a prostatic abscess (patient has fever/chills, elevated WBC, severe tenderness on DRE and fluctuating mass), you would obtain a trans-rectal US.

How is prostatitis classified?

Classic system	NIH classification	
Acute prostatitis	I	Acute prostatitis
Chronic bacterial prostatitis	II	Chronic bacterial prostatitis
Chronic nonbacterial prostatitis	IIIa	Chronic pelvic pain syndrome—inflammatory
Prostatodynia	IIIb	Chronic pelvic pain syndrome—non-inflammatory
	IV	Asymptomatic inflammatory prostatitis

What is your next step?

1. Watch and wait—this is the wrong answer. The patient will develop worsening voiding symptoms and a fever. He could then develop urosepsis and die. This will lead to failure of the case
2. TURP—Transrectal unroofing is indicated to drain a prostatic abscess but is too aggressive in this case and will not treat the patient effectively. If you go this route, the patient will likely develop further complications
3. TRUS biopsy—this is not the time to further investigate the patient's elevated PSA. The patient can develop urosepsis and require admission to the hospital. Pathology will be consistent with prostatitis
4. Antibiotic therapy and supportive therapy—you should institute antibiotic therapy for 4–6 weeks with: Trimethoprim-Sulfamethoxazole (Bactrim DS) 1 tab PO BID or Ciprofloxacin (or other Fluoroquinolone) 500 mg PO BID

In addition you may prescribe a short course of NSAIDS such as Ibuprofen 400 mg PO TID × 5 days, as well as local measures, such as warm sitz baths to alleviate symptoms.

What do you do next?

You need to see the patient back in follow-up to make sure his prostatitis has resolved, as well as follow up on his elevated PSA.

The patient returns 6 weeks later much improved. His voiding symptoms are resolved, and his AUA symptom score is now 3. No other new symptoms.

What do you do now?

Full GU exam including DRE. It is benign, with no nodules. Obtain a UA and repeat the PSA. The UA is WNL and his PSA is 1.1. You discuss the risks and benefits of prostate cancer screening with the patient, and the patient decides to undergo annual DRE and PSA level.

The patient returns 18 months later referred by his PCP. He denies any symptoms but was noted to have a PSA of 2.2 approximately half a year ago and a PSA of 3.3 the previous week.

What do you do?

Although this is an established patient, you have not seen him for over a year. State that you would obtain a thorough history, perform a review of systems, and perform a complete exam. History is non-contributory, ROS is negative, and GU exam including DRE shows a benign; 50 g prostate—smooth, with no nodules.

What studies do you order?

Urinalysis	→	normal
Repeat PSA	→	3.1 ng/mL

What is your assessment

Now 58-year-old CM with a history of chronic prostatitis referred for a rapid rise in his PSA level (elevated PSA velocity).

What is PSA velocity?

PSA velocity is calculated as the PSA rise over a minimum time interval of at least 18 months. Patients with a PSA velocity of 0.75 ng/mL/year have an increased risk of harboring prostate cancer.

What do you do next?

You recommend a transrectal US-guided prostate biopsy.

How do you prepare the patient for the biopsy?

Obtain informed consent, and stop all ASA products or other platelet inhibitors 5–7 days prior to biopsy. Give antibiotics starting the day of the biopsy and 24–72 hours thereafter. Use a periprostatic block to decrease pain.

What are the AUA Antimicrobial Prophylaxis Best Practice Recommendations for TRUS biopsy?

Procedure	Organisms	Prophylaxis Indicated	Antimicrobial of Choice	Alternative Choice	Duration of Therapy
Transrectal prostate biopsy	Intestine	All patients	Fluoroquinolone 1st/2nd/3rd gen Cephalosporin	TMP-SMX Aminoglycoside	24-72 hours

Note: If the choice of antimicrobial is based upon results of a documented rectal swab culture, then culture-directed antimicrobials can be administered.

Source: Wolf JS Jr., Bennett CJ, Dmochowski RR, et al. Best Practice Policy Statement on Urologic Surgery Antimicrobial Prophylaxis. J Urol 2008;179:1379–90 Table 3a. Copyright© 2008 American Urological Association. Published by Elsevier Inc. Used with permission.
(https://www.auanet.org/education/guidelines/antimicrobial-prophylaxis.cfm)

The patient consents to the procedure and you perform an uncomplicated TRUS biopsy with 6 biopsy cores from either side. You send him home with 24 hours worth of

Ciprofloxacin. That night the patient calls you complaining of an elevated temperature of 104° and chills and severe pain in his rectal region.

What do you do next?

Have the patient come to the ER for assessment, obtain urinalysis, urine and blood cultures, and start broad spectrum IV antibiotics.

Urinalysis: nitrite +, large blood, large LE

What is your assessment?

Prostate biopsy induced prostatitis/urosepsis.

Any other measures you would like to take?

Obtain a bladder scan to ensure bladder emptying—PVR: 35 mL.

Start patient on anti-inflammatory such as Ibuprofen to decrease inflammation from prostatitis.

What is the likely organism?

E. coli.

Which antibiotic do you treat with?

Patients presenting with signs of acute infection after TRUS biopsy despite appropriate antibiotic prophylaxis often have organisms resistant to Fluoroquinolones and TMP-SMX. Therefore, place patient on broad spectrum coverage such as Ampicillin + Gentamicin.

What are the AUA White Paper Risk Factors for Post-Prostate Biopsy Infectious Complications?

Recent antimicrobial exposure, hospital employees and their family members, and recent international travel.

Urine culture shows >100K E. coli resistant to Ciprofloxacin, but sensitive to TMP-SMX. Blood cultures were negative. The patient does well and goes home after 36 hours in the hospital, and you send him out on TMP-SMX for 4 weeks to treat prostatitis.

What is your follow up?

Ask for the pathology report. The path report indicates Gleason 3 + 4=7 adenocarcinoma of the prostate in 2/12 cores with multiple cores showing chronic prostatitis. The patient ultimately undergoes an uncomplicated nerve-sparing radical prostatectomy and thanks you for your excellent care.

CHAPTER 9

STONE DISEASE

BRANDON OTTO, MD
BENJAMIN CANALES, MD

CASE 1

HPI: 39-year-old female presents to the emergency room with fever, chills, nausea, and vomiting associated with an acute onset of right flank pain. The pain radiates towards her right lower quadrant. She reports increasing urinary frequency and urgency and denies gross hematuria.

PMH: none

PSH: none

Allergies: IV contrast (hives) **Medications:** none

SH: (-) tob; (+) ETOH, rare use
FH: mother with breast cancer
ROS: (-) except for above

PE:

Vitals: T 103 P 110 BP 100/60 O2 99% on RA
General: ill-appearing in moderate distress
Abdomen: soft; mild RLQ tenderness to palpation; no guarding; no rebound
Back: right CVAT

Labs:

UA → 5 RBC/HPF; 5 WBC/HPF; + nitrite; + LE, moderate bacteria
CBC → WBC 14 K/µL with bands and left shift
Chem 7 → WNL
hCG test → negative

What is your differential diagnosis?

Nephrolithiasis, pyelonephritis, ovarian pathology, GI pathology (appendicitis).

What is your initial imaging study of choice?

In the setting of a suspected renal colic, a non-contrasted, spiral CT scan (stone protocol) is the imaging modality of choice. Obtain additional KUB as a reference for future follow-up.

CT scan: 1 cm (R) distal ureteral calculus; radiopaque, (R) moderate hydronephrosis; normal appearing contralateral kidney
KUB: 1 cm (R) distal ureteral calculus; radiopaque

Note: Must specifically ask for the results of the pregnancy test before proceeding with radiographic imaging and check a serum Cr level if considering intravenous contrast.

What alternative imaging studies would you consider?

If Cr WNL → CT abdomen and pelvis with and without contrast with delayed images. Use non-ionic contrast agent and administer steroid prep. Note that the administration of IV contrast will delay the diagnosis

If pregnant → renal or transvaginal ultrasound. MRI (useful for ruling out other pathologies of pregnancy that can mimic a renal colic) or limited IVP (KUB + 15 min film) with precautions as outlined above

What is your assessment?

39-year-old F with fever and obstructing (R) distal ureteral stone.

What is your initial treatment?

1. First stabilize the patient with IVF, antibiotics, antiemetics and pain medication. Give broad spectrum intravenous antibiotics after cultures obtained (i.e., Ampicillin and Gentamicin)

   Note: Do not proceed with surgery without giving antibiotics first. (Management of ureteral calculi: EAU/AUA nephrolithiasis panel: standard)

2. Schedule urgent cystoscopy, (R) retrograde pyelogram and stent placement

   Note: Do not extract the stone at the time of stent placement in a febrile patient. Be safe!

3. If you are unable to place a stent or the patient is not a candidate for anesthesia, have the interventional radiologist place a percutaneous nephrostomy tube

What are some of the indications for prompt stone intervention?

1. Any degree of obstruction in an infected or suspected infected kidney
2. Any degree of obstruction in a solitary kidney
3. Complete or high grade unilateral urinary obstruction or any degree of bilateral urinary obstruction
4. Any degree of obstruction with a rising Cr
5. Inability to tolerate PO secondary to nausea/vomiting
6. Pain not controlled by oral analgesics

Case follow-up:

A right ureteral stent was placed successfully. Blood cultures were negative; however, her urine culture grew E. coli. The patient was discharged home on antibiotics, pain medication, and given a urine strainer.

She returns to your office in 2 weeks and states that she has not passed the stone. She is having persistent (R) flank pain. Physical exam demonstrates right CVAT. A repeat KUB shows a 1 cm right distal ureteral calculus with the stent in good position. A repeat urine culture is negative.

What are your treatment options?

Patients must be informed about existing active treatment modalities, including the relative benefits and risks associated with each modality. SWL and URS should be discussed as the initial treatment options for ureteral stones. Discussion should include stone-free rates, anesthesia requirements, need for additional procedures and associated complications.

1. Ureteroscopy with stone manipulation under fluoroscopy using various treatment modalities. Stone free rate (SFR) for distal ureteral stones ≥ 10 mm is 93% with ureteroscopy
   a. Electrohydraulic lithotripsy (EHL)
      i. This therapy is based on the shockwave principle

        - ii. The EHL fiber needs to be 1 mm from the stone
        - iii. Use normal saline irrigation
        - iv. EHL may be used with rigid and flexible ureteroscopes
        - v. Risk: It may easily perforate the ureter—not the primary treatment option if other modalities are available
    - b. Lithoclast
        - i. Good for distal ureteral stones
        - ii. Lithoclast can only be used with rigid ureteroscopes
        - iii. Risk: there is "cueballing" effect
    - c. Holmium laser
        - i. Holmium is excellent for treating all types of stones
        - ii. It will fragment the stone into small particles
        - iii. Holmium laser fiber may be used with rigid and flexible ureteroscopes
        - iv. Risk: Holmium laser may perforate the ureter upon direct contact

    Note: Never state that you perform blind stone basketing! (Management of ureteral calculi: EAU/AUA nephrolithiasis panel: standard).

    Note: Do not perform ureteroscopy without placing a safety wire first.

2. Shock wave lithotripsy
    - a. Not the best treatment option given the stone size and location (SFR for distal ureteral stones ≥ 10 mm is 74% with SWL)
    - b. Increased risk of repeat primary procedures/secondary procedures (frequency: 1.37)
    - c. Also relatively contraindicated in a female patient of reproductive age; however, can be performed with IV sedation/other minimal anesthetic techniques; routine stenting is not recommended
3. Medical expulsive therapy: an option if patient would like to delay procedure; however, given size of stone, likelihood of spontaneous passage is low

The patient chooses ureteroscopy.

How do you proceed?

Obtain informed consent, order preoperative labs, including a repeat urine culture, and give preoperative antibiotics.

She underwent ureteroscopy with Holmium laser lithotripsy and stone basketing without complications. A new stent was placed after the stone was removed.

Note: Stenting following uncomplicated URS is optional (management of ureteral calculi: EAU/AUA nephrolithiasis panel: option).

What are the possible complications of ureteroscopy for distal ureteral stones?

1. UTI (4%)
2. Ureteral injury (3%)
3. Sepsis (2%)
4. Stricture (1%)

What is your follow-up?

She needs chemical analysis of the stone that was extracted and metabolic evaluation. Don't forget to discuss importance of adequate hydration and dietary modification.

1. Stone analysis
2. Screening evaluation for a patient with newly diagnosed kidney or ureteral stones
   a. Detailed medical and dietary history to elicit any medical conditions, medications or dietary habits that predispose to stone disease
      i. Medical history: obesity, hyperthyroidism, gout, RTA type 1, DM type 2, bone disease, hyperparathyroidism, malabsorptive GI states (bowel resection, bariatric surgery, pancreatic disease)
      ii. Medications: Probenecid, Protease inhibitors, Lipase inhibitors, Triamterene, chemotherapy, vitamin C, vitamin D, calcium and Carbonic anhydrase inhibitors
      iii. Dietary history: average daily intake of fluids (amount and type), protein (types and amounts), calcium, sodium, high oxalate-containing foods, fruits and vegetables, over-the-counter supplements
   b. Serum chemistries: electrolytes, calcium, creatinine and uric acid
   c. Urinalysis: dipstick and microscopic evaluation to assess urine pH, indicators of infection (if positive obtain urine culture), and to look for crystals
3. Additional metabolic testing should be performed in high-risk or interested stone formers
   a. Same as above + parathyroid hormone level
   b. 1 or 2 24-hour urine collections obtained on a random diet and analyzed for: total volume, pH, calcium, oxalate, uric acid, citrate, sodium, potassium and creatinine. Can look for cystine in patients with cystine stones or a family history of cystine stones

   Note: Metabolic evaluation should be performed in a non-acute setting at 1 month after passage of the stone or stone extraction.

4. Discuss prevention with hydration (increase fluid intake to achieve a urine volume of at least 2.5 L/day)
5. Remove stent in 1–2 weeks; document stone passage by KUB at the time
6. Obtain imaging with renal US at 6–12 weeks to document stone removal and absence of obstruction (residual/recurrent stone, ureteral stricture as complication of ureteral instrumentation)

CASE 2

HPI: 57-year-old female presents to the clinic complaining of chronic low back pain and recurrent urinary tract infections. She reports several documented positive cultures over the past year with P. mirabilis. She denies gross hematuria and has no history of kidney stones.

PMH: (-) except for above

PSH: none

Allergies: NKDA **Medications:** ASA 81 mg

SH: (-) tob; (+) ETOH, social
FH: (+) mother and father CAD
ROS: (-) except for above

PE:

Vitals:	T 98.1	P 75	BP 120/65	O2 99% on RA
General:	no acute distress			
Abdomen:	soft, NTND			
Back:	(-) CVAT			
GU:	unremarkable			

Labs:

UA → 5 RBC/HPF; 3 WBC/HPF; (-) nitrite; (-) LE, no bacteria, no casts
UCx → negative
CBC → WNL
Chem 7 → Cr: 1.6 mg/dL

What is your next step?

Patient has microscopic hematuria and recurrent UTIs.

1. Microscopic hematuria (≥3 RBC per HPF on UA with microscopy): she will need assessment as she has persistent microscopic hematuria in the absence of a current infection. Microscopic hematuria on patients taking anticoagulants still needs to be evaluated
    a. Creatinine
    b. Cystoscopy (all patients with microscopic hematuria aged >35)
    c. Upper tract imaging
    d. Cytology is NOT recommended during routine evaluation
2. Recurrent UTIs (≥3 culture proven infections/12 months or ≥2 in 6 months)
    a. History (number and frequency of infections, temporal associations (intercourse), menopausal status, recent antibiotic use, sexual history, pneumaturia or fecaluria)
    b. Physical exam: quality of vaginal epithelium, pelvic organ prolapse, urethral diverticulum
    c. PVR
    d. Consider cystoscopy and upper tract imaging for UTIs that are complicated, persistent or frequent

She underwent a cystoscopy which was normal. Her PVR was 25. A CT urogram demonstrated an 8 cm left partial staghorn calculus. There was no hydronephrosis. The left kidney appeared smaller than the right kidney and has less parenchyma.

Does she need any functional studies of the kidney?

Note: Need to obtain a functional study prior to treatment.

Nuclear renal scan → 35% function on (L); 65% function on (R)

What is your assessment?

57-year-old F with non-obstructing (L) partial staghorn calculus.
Left kidney has relatively good function and should be saved.

What are your treatment options?

The goal of therapy is complete removal of the stone, and there are 4 treatment strategies:

1. Percutaneous nephrolithotomy (PCNL) (SFR 78%)
2. Combinations of PCNL and SWL (SFR 66%)
3. SWL monotherapy (SFR 54%)
4. Open surgery (SFR 71%)

Initial treatment of choice in this patient is likely PCNL; it has the highest SFR and the lowest number of total procedures performed (PCNL: 1.9, combination therapy: 3.3, SWL: 3.9).

SWL monotherapy should not be used for most patients. If it is performed, adequate drainage of the kidney should be established prior to the procedure.

Open surgery is rarely necessary today.

How would you proceed?

1. First obtain an informed consent. State that you would discuss the surgical procedure, indications, potential risks, and complications
2. State that you would get appropriate preoperative work up; CXR, EKG, and labs—especially PT, PTT, and platelets. Bleeding time as necessary
3. Type and screen patient
4. Give broad spectrum IV antibiotics (i.e., Ampicillin and Gentamicin) preoperatively. Depending on sensitivity, consider preoperative (suppressive) antibiotics orally or via PICC-line

   Note: Urine culture must be negative prior to treatment.

5. Percutaneous access may be obtained by the interventional radiologist or by you on the day of the operation. The calyx of entry and the number of calyceal accesses depend on intrarenal anatomy and the relative position of the stone within the collecting system

   Note: Uncorrected coagulopathy, active UTI and pregnancy are contraindications to PCNL.

Describe your surgical technique:

Be prepared to discuss the actual operative procedure.

The Operation (traditional PCNL)

1. Insert a Foley catheter
2. Place the patient in a prone position
3. Pad all pressure points
4. Obtain access and place 2 guide wires into the bladder (i.e., safety wire and working wire)
5. Dilate the tract under fluoroscopy (Amplatz dilator or balloon)
6. Remove all stone fragments (ultrasound probes, lithoclast, EHL or Holmium laser)
7. Perform nephrostogram to rule out injury to renal pelvis or ureter
8. Place antegrade stent
9. Insert nephrostomy tube

Discuss intraoperative complications and management:

1. Venous bleeding → Stop the operation
   Place and inflate the nephrostomy tube in the renal pelvis to tamponade the bleeding
2. Arterial bleeding → Foley catheter (nephrostomy tube) tamponade and clamp
   Stop the procedure
   Possible embolization
   AVF = artery and vein injury (distal ischemia from where arterial blood is supposed to go; remember, kidney has end arteries)
3. Stone migrated out of the renal pelvis → Leave it alone
4. Significant tear in the renal pelvis → Stop the operation
5. Irrigation mismatch → If irrigant loss is more than 1000 mL, stop the operation

Discuss your postoperative management.

1. Obtain a CXR in the recovery room to rule out a pneumothorax
2. Antegrade nephrostogram if urine clear (POD #1 or #2)
3. Clamp and remove the nephrostomy tube if there is no evidence of extravasation or residual stone that would necessitate a second look procedure
4. Remove the JJ stent as an outpatient

She did well from her surgery and stone analysis revealed struvite stone.

What are some adjunctive options to PCNL?

1. PCNL + SWL
   a. Any significant residual stone fragments can be broken up with ESWL
2. PCNL + ESWL + PCNL ("Sandwich Technique")
   a. Significant residual stone fragments are broken up with ESWL and stone fragments are removed via percutaneous approach
   b. If combination therapy is performed, PCNL should be the last procedure for most patients
3. PCNL + chemolysis (insufficient evidence to be included in guidelines)
   a. Struvite → Renacidin; Hemiacidrin; Suby's Solution G

What is a struvite stone?

Struvite stone is an infection stone composed of magnesium, ammonium, and phosphate with small quantities of calcium phosphate mixed in the lattice. Presence of urea and urease are essential to struvite stone formation. Bacteria such as Proteus, Klebsiella, Pseudomonas, and Staphylococcus epidermidis contain urease enzyme that converts urea into bicarbonate and ammonia.

Urea → bicarbonate and ammonia → alkaline urine

How do you medically treat struvite stone?

1. Adequate hydration → increase urine volume to > 2 liter (2 quarts)/day
2. Acetohydroxamic acid → urease inhibitor urine; side effects: neurologic, hematologic, and teratogenic. May recommend only after surgical options have been exhausted

CASE 3

HPI: 27-year-old G1P0 (1st trimester) female is referred to you by her PCP for a 2.5 × 1.5 cm right renal pelvis stone with moderate hydronephrosis. The stone was discovered on evaluation for recurrent right flank pain. The patient denies fever, chills, nausea and vomiting. The patient endorses increased urinary frequency, denies gross hematuria. The patient was treated for a ureteral calculus 6 months ago with ureteroscopy and stone extraction. Stone analysis revealed a cystine stone. The patient is requesting an ESWL.

PMH: none

PSH: as above

Allergies: NKDA **Medications:** prenatal vitamin

SH: (-) tob; (-) ETOH
FH: + cystine stones
ROS: (-) except for above

PE:

Vitals:	T: 98.3	P 65	BP: 108/62	O2: 99% on RA
General:	no acute distress			
Abdomen:	soft; NTND; uterine fundal height appropriate for gestational age			
Back:	mild R CVAT			

Labs:

UA	→	pH 6; hexagonal crystals
UCx	→	negative
CBC	→	WNL
Chem 7	→	WNL; Cr 0.8 mg/dL

What is your assessment?

27-year-old pregnant F with obstructing cystine stone in (R) renal pelvis.

What are your treatment options?

Options include expectant management with symptomatic treatment, placement of a nephrostomy or double J drainage, ureteroscopy with stone fragmentation and PCNL.

Discuss your best treatment option and why.

1. Stone will likely not pass spontaneously; however, a trial of conservative management with hydration and analgesia as needed is an optional first line treatment
2. SWL is wrong
    a. The stone is too large and pregnancy is a contraindication to SWL
    b. Furthermore, cystine stones are very difficult to fragment by SWL
3. For management of persistent symptoms or obstruction, upper tract drainage with a ureteral stent or nephrostomy is indicated
    a. Stents and nephrostomies should be exchanged every 6 weeks due to the risk of rapid encrustation

    b. For patients presenting early in pregnancy, PCNs obviate the need for frequent operative stent changes
4. PCNL is rarely indicated during pregnancy
5. Treatment of choice in this patient is placement of JJ stent or nephrostomy and oral alkalinization
    a. Urine pH: alkalinize urine to pH 7 with potassium citrate
    b. Hydration: fluid intake sufficient to reduce urine concentration of cystine below solubility limit of 200–250 mg/dL

Note: Over-alkalinization can lead to calcium phosphate formation.

She wants to go ahead with placement of an internal stent.

How do you proceed?

Obtain informed consent, order preoperative labs including a urine culture, and give IV antibiotics. Discuss possibility of fetal loss.

Cystoscopy was performed. Internal stent was placed under ultrasound guidance and oral alkalinization was instituted. She carried the fetus to term and delivered a healthy baby boy.

What are postpartum treatment options?

After delivery, proceed with PCNL.

This patient originally wanted a SWL. She is again requesting SWL.

What are the absolute and relative contraindications of SWL?

Absolute contraindication of SWL	Relative contraindication of SWL
Acute infection	Cystine stone
Uncorrected coagulopathy	Calcium oxalate monohydrate stone
Pregnancy	Obesity (skin to stone >10 cm)
Distal obstruction	Stone size and location

Note: Cystine stone and calcium oxalate monohydrate stones are relatively contraindicated for SWL because they are extremely hard stones that do not fragment easily with shockwave lithotripsy. Lower pole stone success rate is lower with SWL especially if infundibulum is long (>10 mm), narrow (<5 mm) or the infundibulopelvic angle is <90°.

What is the pathophysiology of cystine stone?

Cystine stone occurs due to inborn error of metabolism. Affected patients are unable to reabsorb cysteine, ornithine, lysine, and arginine (COLA). Ornithine, lysine, and arginine are soluble in urine but cystine is not.

Cystine stones form when two cysteine molecules join via a disulfide bond. Cystinuria is inherited as autosomal recessive trait. Only homozygous recessives are stone formers. On urinalysis, hexagon crystals are seen.

How do you diagnose cystine stones?

Presence of cystine stone is suggested by radiolucent filling defect, hexagon crystals on urinalysis, and acidic urine pH. However, cystine stone is diagnosed by positive cyanide-nitroprusside test and stone analysis.

How do you prevent cystine stones?

Adequate hydration	→	increase urine volume to raise solubility
Low methionine diet	→	very unpalatable, poor compliance
Low sodium diet	→	decreases cysteine excretion by kidney
Sodium bicarbonate	→	raise urine pH to 7 (increases cysteine excretion)
Potassium citrate	→	raise urine pH to 7
Acetazolamide	→	raise urine pH to 7
D-penicillamine	→	binds cystine, forming a complex that is soluble, give with vitamin B6 (pyridoxine). GI side effects, impairment of taste and smell, dermatologic complications (urticaria and pemphigus), hypersensitivity reactions, arthralgia, hematologic side effects
α-MCPG	→	similar to D-penicillamine. Better tolerated

During thiol therapy (D-penicillamine and α-MCPG), it is important to check LFTs, serum albumin, CBC, 24-hour urine for protein and cystine, UA and urine pH every 3–6 months. These drugs should be offered to patients with cystine stones who are unresponsive to dietary modifications and urinary alkalization or have large recurrent stone burdens.

How do you treat cystine stones?

Large or symptomatic stones	→	manage in usual fashion (PCNL versus URS)
Small stones	→	attempt dissolution with potassium citrate to pH of 7

The patient underwent a successful PCNL and was maintained on alkalization therapy post-operatively.

CASE 4

HPI: 55-year-old African-American male with a PMH of nephrolithiasis presents to the clinic complaining of right renal colic and an episode of gross hematuria. The pain occurred 3 days ago and radiated to his groin. The gross hematuria has resolved. His prior stones passed spontaneously. He has never had a stone analyzed.

PMH: as above

PSH: none

Allergies: NKDA **Medications:** none

SH: (+) tob, smoked for a few years in college; (-) ETOH
FH: (-)
ROS: (-) except for above

PE:

Vitals: T 97.8 P 74 BP 140/70 O2 99% on RA
General: no acute distress
Abdomen: soft, NTND
Back: mild R CVAT

Labs:

UA → pH 5; 10 RBC/HPF; (-) WBCs
UCx → negative
CBC → WBC 11 K/μL
Chem 7 → WNL

Imaging:

KUB → (-) radiopaque calcifications
IVP → (R) UPJ filling defect @ 1 cm; moderate hydronephrosis
CT scan → 1 cm (R) UPJ stone with moderate hydronephrosis on non-contrast CT scan

Other:
Cystoscopy: → normal bladder; (-) tumors, stones, or CIS

What is your assessment?

55-year-old AAM with a PMH of nephrolithiasis now with right renal colic secondary to a 1 cm right UPJ radiolucent calculus and moderate hydronephrosis. He most likely has a uric acid stone since his urine pH is 5 and the stone is radiolucent.

What are your treatment options?

1. Placement of JJ stent and oral alkalinization
    a. Prescribe potassium citrate to maintain a urine pH of ≥6

2. Primary ureteroscopy with laser lithotripsy for patients who do not want to be on or cannot tolerate potassium citrate
3. Alternative is to perform SWL after stent placement followed by oral alkalinization

The patient chooses stent placement and oral alkalinization. The stone dissolves and his stent is removed. 6 weeks after his stent was removed he underwent a full metabolic evaluation. His serum uric acid was elevated and he was found to have hyperuricosuria (>800 mg/day).

Are there any other additional therapies to consider?

1. If serum uric acid is high, prescribe Allopurinol 300 mg QD
2. If he has hyperuricosuria, he will also benefit from Allopurinol
3. His diet should be low purine diet and hydration should be increased to produce 2.5 liters of urine/day. He needs to decrease his intake of red meat, chicken, etc.

What are some clinical causes of uric acid stone formation?

1. Gout
2. Ileostomy, chronic diarrhea (as conditions resulting in dehydration and acidic urine)
3. Myeloproliferative disorders, tumor lysis
4. Uricosuric drugs
    a. Probenecid, Salicylates
    b. Thiazide, Sulfinpyrazone
5. Lesch-Nyhan syndrome
    a. Hyperuricemia/hyperuricosuria
    b. Deficiency in hypoxanthine guanine phosphoribosyltransferase (HGPRT)
    c. Self-mutilation

What are some clinical indicators of uric acid stone?

1. Acidic urine
2. Radiolucent filling defect on IVP
3. Needle-shaped crystals in urine

What are some risk factors for uric acid stone formation?

1. Acidic urine
2. Hyperuricosuria
3. Dehydration

How do you treat uric acid stone?

1. Adequate hydration → increase urine volume to > 2.5L/day
2. Low uric acid diet → avoid red meat, poultry, peanuts
3. Sodium bicarbonate → alkalinize urine; raise pH to ≥6
4. Potassium citrate → alkalinize urine; raise pH to ≥6

Note: If urine pH is too high, calcium apatite stone may form.

5. Allopurinol → xanthine oxidase inhibitor; recommended for patients with hyperuricemia/extreme hyperuricosuria

CASE 5

HPI: 54-year-old African-American female presents to the clinic complaining of recurrent urinary tract infections. She reports multiple episodes of acute cystitis over the past 2 years and 1 episode of pyelonephritis 3 months ago. She denies any history of nephrolithiasis and has no UTI symptoms now. No flank pain, gross hematuria or incontinence. A PVR in the office was 15.

PMH: asthma; rheumatoid arthritis; chronic low back pain

PSH: tubal ligation

Allergies: Penicillin (unknown reaction) **Medications:** ASA 81 mg, Albuterol inhaler

SH: (-) tob; (-) ETOH
FH: (-)
ROS: (-) except for above

PE:

Vitals: T 98.1 P 80 BP: 125/75 O2: 97% on RA
General: obese AAF
Abdomen: soft; NT/ND
Back: mild R CVAT
GU: unremarkable

Labs:

UA → pH 8; 4–12 RBC/HPF; 10–20 WBC/HPF; nitrites (+); leukocyte esterase (+); phosphate crystals
UCx → > 100,000 Proteus mirabilis; pan-sensitive
CBC → WNL
Chem 7 → WNL; Cr 1.3 mg/dL

What would you do first?

State that you would treat UTI first with oral antibiotics. Important to repeat a UA after UTI treated to see if microscopic hematuria resolved.

Note: She is allergic to PCN.

You prescribed Ciprofloxacin for 3 days for simple cystitis. After the 3 days of antibiotic therapy, urine culture reveals no growth of bacteria.

The patient was treated with a course of Ciprofloxacin. A repeat urine culture shows no growth; however, her repeat UA revealed 13–25 RBC/HPF.

How would you proceed?

You would proceed by completing her microscopic hematuria work-up with a cystoscopy and upper tract imaging.

Her cystoscopy was normal and imaging revealed a 10-cm branched right staghorn calculus with delayed excretion of contrast from the right kidney. The left kidney appeared normal.

Are there any other radiologic tests that you would perform?

Renal scan:	40% function (R) kidney 60% function (L) kidney

Note: Need to assess renal function.

What is your assessment?

54-year-old AAF with (R) staghorn calculus.

What are your treatment options?

You must be able to discuss pros and cons of SWL, PCNL, and sandwich therapy with your patient. You must choose an operation that you are able to perform. If you are unable to perform such an operation, your examiner will want you to describe it at least in theory. See CASE 2 for more information regarding SFR and retreatment rates.

1. PCNL
   a. Percutaneous nephrolithotomy is an excellent treatment option for large stones
   b. Treatment of large stone burdens may require multiple access tracts, although this is associated with an increased risk of complications (i.e., pneumothorax, nephropleural fistula, or injury to adjacent organs)
2. SWL monotherapy
   a. Stones < 1.5 cm in diameter are suitable for SWL
   b. Stone burden > 2 cm will require multiple procedures due to problems with passing gravel and steinstrasse formation
3. Sandwich therapy (PCNL+SWL+PCNL)
   a. Sandwich therapy refers to PCNL followed by SWL and repeat PCNL
   b. After percutaneous lithotripsy of a large branched staghorn calculus, several large fragments may remain
      i. This residual stone burden is fragmented into smaller pieces by using SWL therapy
      ii. The remaining smaller fragments are then plucked out via originally created percutaneous tract
4. Open stone surgery

You recommend PCNL and the patient agrees.

Discuss your surgical technique.

See CASE 2

Discuss adjacent organ injury and management.

1. Colon injury
   a. Place stent and pull nephrostomy tube back into the colon
   b. Give antibiotics. General surgery consult
   c. Pull out the nephrostomy tube when the kidney has healed
2. Duodenal injury
   a. General surgery consult, antibiotics, TPN, NGT, Gastrografin swallow
3. Liver injury
   a. Monitor with vitals and serial Hgb
   b. Staging by dedicated CT scan and general surgery consult
   c. If there is persistent bleeding, explore the abdomen

4. Spleen injury
   a. General surgery consult
   b. Small injury → monitor
   c. Large injury → splenectomy
5. Pleural injury with hydrothorax
   a. Drain with chest tube
   b. Divert urine with double J or PCN
   c. Obtain serial CXR

On POD #1, an antegrade nephrostogram shows no extravasation, but there was a residual fragment in the upper pole of the right kidney. The patient was discharged to home on POD #2 and a follow-up KUB showed a 7 mm residual fragment in the renal pelvis.

How do you proceed?

You discuss further management options, which include watchful waiting, SWL and repeat PCNL. You recommend SWL to fragment the residual stone. Repeat PCNL is also a good alternative option since you already have an access tract in place.

The patient agrees to SWL, which results in good stone fragmentation.

What are the reported complications of SWL?

1. Hematuria/perinephric hematoma → need to admit, observe and monitor hemodynamics; transfuse as necessary
2. Residual stones → need to obtain KUB, IVP, or renal US
3. HTN → need to monitor BP during the first year
4. Sepsis → rule out UTI prior to treatment; administer prophylactic antibiotics
5. Steinstrasse/obstruction → may require stent/PCN placement

What are the effects of shock rate and voltage setting on SWL success?

Treatment success is better when using a lower shock rate (60–90 shocks/minute) compared to a higher shock rate (120 shocks/minute). Voltage should be increased in a stepwise fashion from a lower to higher kilovolt setting. Both strategies improve treatment success and decrease risk of renal injury.

What is your follow-up?

1. Prophylactic antibiotics depending on urine culture and sensitivities
2. Follow-up KUB
3. Removal of PCN
4. Functional study (IVP or CT scan without/with contrast within 3 months to document stone clearance and absence of obstruction)

1 year later she returns complaining of right flank pain. She had an acute onset of pain while working. The pain is colicky and radiates to her right groin. She denies fever, chills, nausea and vomiting. She has right CVAT. A non-contrast CT demonstrated an 8 mm distal right ureteral stone with moderate hydronephrosis. A urine culture is negative.

Given her uncontrolled pain, the patient was admitted and a right ureteral stent was placed. 1 month after stent placement, she continues to have flank pain and is tolerating the stent poorly. A KUB documents a persistent stone.

How do you proceed?

State that you would perform ureteroscopy and stone fragmentation.
You must be able to discuss the management of complications of ureteroscopy.
Alternatively, you might recommend SWL. The SFR was distal ureteral stones <10 mm are 86% for SWL and 97% for URS. See CASE 1 for more information about complications of URS.

The patient elects to undergo ureteroscopy with laser lithotripsy. You manage to successfully fragment the ureteral calculi. However, your partner decides to blindly stone basket the stone fragments against your advice. During basketing of the stone, your partner avulses the distal ureter. You could not successfully place a stent. You looked for interventional radiologist to place a nephrostomy tube, but he was on vacation.

What are your surgical options?

1. Ureteroureterostomy—useful for injury to midureter
2. Nephropexy and ureteroureterostomy—useful for injury to upper and midureter
3. Ureteroneocystostomy—useful for injury to distal ureter
4. Psoas hitch—useful for injury to distal ureter
5. Boari flap—useful for injury to mid to distal ureter
6. Ileal ureter—useful for correcting significant loss of ureteral length
7. Autotransplant—this is the last resort for saving the kidney if all attempts at ureteral reconstruction fail
8. Nephrectomy

Note: Recurrent calculus formation is a contraindication for TUU.

Your patient had a distal ureteral avulsion, but the ureter is too short to perform a primary ureteral re-implant. You have to perform a psoas hitch and may need a Boari flap.

Discuss your surgical technique:

The Operation (Psoas hitch)

1. Make a midline or Pfannenstiel incision
2. Mobilize the bladder
3. Ligate superior and middle vesical artery on contralateral side to gain mobility
4. Make anterior vertical cystotomy
5. Insert a finger into the dome of the bladder and elevate it to the anterior surface of the ipsilateral psoas muscle
6. Affix the dome of the bladder to the fascia of the psoas with 2-0 PDS sutures
7. Avoid genitofemoral nerve
8. Prepare the ureter
    a. Bring the ureter through the dome of the bladder
    b. Either anti-refluxing tunnel or refluxing end-to-end anastomosis may be performed
9. Ureter should lie straight and without tension
10. Place a ureteral stent
11. Leave a Foley catheter

The Operation (Boari flap)

1. Create a bladder flap.
    a. The flap is based on posterior lateral wall on the side of proposed ureteroneocystostomy
    b. The length of the flap depends on the distance between the posterior lateral wall and the distal ureter
    c. The width of the base of the flap should be at least 2 cm > the apex
2. Mobilize the flap toward the distal end of the ureter. Tubularize the flap
3. Perform ureteroneocystostomy
    a. Either anti-refluxing tunnel or refluxing end-to-end anastomosis may be performed
4. Insert a stent. Place Foley catheter, SPT, and drain
5. Close the incision

What are the Do's and Don'ts of ureteroscopy?

1. Do have a safety wire in place prior to stone manipulation
2. Do inform patient of possible open ureteral surgery
3. Do remove the stent postoperatively
4. Do stop the procedure when ureteral perforation occurs
5. Don't state that you perform blind stone basketing

CASE 6

HPI: 55-year-old Caucasian male complains of the acute onset of L flank pain 3 days ago. He had 1 episode of gross hematuria. He denies fevers and chills but does have nausea and vomiting. He denies any urinary symptoms. He has passed 2 stones spontaneously during his lifetime.

PMH: as above

PSH: bilateral inguinal hernia repair

Allergies: NKDA **Medications:** none

SH: (-) tob; (-) ETOH
FH: (-)
ROS: (-) except for above

PE:

Vitals: T 98.6 P 120 BP 140/80 O2: 99% on RA
General: moderate distress
Abdomen: soft, NTND
Back: L CVAT

Labs:

UA → pH 6.5; 2–3 WBC/HPF; 10–15 RBC/HPF; (-) bacteria; (-) crystals
UCx → no growth
CBC → WBC 11 K/μL
BMP → Cr 1.1 mg/dL

Imaging:

KUB → 1.0 cm radiopaque calculus in (L) upper quadrant
CT scan → 1.0 cm radiopaque calculus in the (L) proximal ureter with partial ureteral obstruction and mild hydronephrosis; normal appearing contralateral kidney

What is your assessment?

55-year-old CM with a 1 cm left proximal ureteral stone and mild hydronephrosis.

After stabilizing the patient, you discuss treatment options such as medical expulsive therapy versus surgical intervention. He opts to undergo medical expulsive therapy since he has passed his prior stones without intervention.

What is medical expulsive therapy?

Medical expulsive therapy (MET) is a strategy to improve spontaneous stone passage. The patient is given an α-blocker to facilitate stone passage.

α-blockers increase the stone passage rate by approximately 29%, decrease the time to stone passage by 2–4 days and decrease pain during stone passage. Calcium channel blockers and steroids have also been studied but are generally less effective than α-blockers.

Patients should be counseled on the attendant risks of MET, including the side effects of an α-blocker and that it is being administered for an "off label" use.

Patients on MET should be followed with periodic imaging studies to monitor stone position and to assess for hydronephrosis.

What is the incidence of spontaneous passage of ureteral calculus?

Stone size		Spontaneous passage rate		Typical treatment
Stone < 4 mm	→	90%	→	Observation
Stone 4–6 mm	→	50%	→	Sometimes surgery
Stone > 6 mm	→	10%	→	Usually surgery

What are indications for intervention in a patient on MET?

1. Poorly controlled pain
2. Persistent nausea/vomiting
3. Fever, leukocytosis, bacteriuria
4. Rising Cr
5. Worsening obstruction
6. Stone fails to progress
7. Patient preference

What are the sites of ureteral obstruction for stones?

UVJ / UPJ /crossing of iliacs.

After 4 weeks, a repeat KUB shows that the stone has not moved and remains at the left UPJ. Your patient is anxious to have this stone taken care of and desperately wants something done. You recommend an SWL which fails to break up the stone.

What type of stone do you think it is?

The stone is probably composed of calcium oxalate monohydrate.

What do you recommend next?

Ureteroscopy and laser lithotripsy with stent placement.

He tolerated the procedure well without complications and was transferred to the recovery room. He recovers uneventfully from surgery.

What is your follow-up?

Remove the stent and review stone analysis.

Note: Need to ask for stone analysis.

Stone analysis: calcium oxalate monohydrate

Name specific stones and their incidence.

1. Calcium (oxalate/phosphate)	70%
2. Struvite	15–20%
3. Uric acid	5–10%
4. Cystine	1–5%

What would you offer next for this patient?

Metabolic evaluation for stone formation.

What is the timing of metabolic stone evaluation for a patient who recently passed a stone?

Ideally this is done 1 month after resolution of ureteral obstruction, infection, or stone extraction.

His metabolic stone evaluation is notable for hypercalciuria.

What dietary recommendations should you make for him?

1. Limit sodium intake to ≤100 mEq (2,300 mg) daily
2. Consume 1,000–1,200 mg/day of dietary calcium
3. Thiazide diuretics (HCTZ, Chlorthalidone and Indapamide) reduce formation of recurrent calcium stones. Limiting sodium intake helps improve hypocalciuric effect

What pharmacologic therapy could you consider?

Potassium supplementation may be required if hypokalemia develops.

What if his metabolic stone evaluation was notable for hyperoxaluria? What dietary recommendations should you make for him?

1. Limit intake of oxalate-rich foods
2. Consume 1,000–1,2000 mg/day of dietary calcium

What if his metabolic stone evaluation was notable for relatively low urinary citrate?

1. Increase intake of fruits and vegetables
2. Limit non-dairy animal protein

What dietary recommendations should you make for him?

Potassium citrate (may also be beneficial in patients with normal urinary citrate but low urine pH). Increasing pH too much may shift stones from CaOx to calcium phosphate.

What if his metabolic stone evaluation was notable for high urinary uric acid. What dietary recommendations should you make for him?

Limiting non-diary animal protein may help reduce stone recurrence.

What pharmacologic therapy could you consider?

Allopurinol has been shown to decrease stone formation in patients with hyperuricosuria (>800 mg/day) and normocalciuria.

What pharmacologic therapies can you consider in recurrent calcium stone formers with no metabolic abnormalities?

Thiazide diuretics and/or potassium citrate have both been shown to prevent recurrent stones in patients with normal range urinary calcium and citrate respectively.

After instituting dietary and/or pharmacotherapy, how and when should a clinician assess for a response to therapy?

1. A single 24-hour urine specimen within 6 months
2. After the initial follow-up, clinicians should obtain a single 24-hour urine specimen annually or with greater frequency, depending on stone activity to assess patient adherence and metabolic response

CASE 7

HPI: 46-year-old female presented to the emergency room with fever, dysuria and flank pain. She initially had irritative LUTS and hematuria starting 5 days ago. The hematuria resolved after 2 days. She then began having right flank pain associated with nausea and vomiting 3 days ago. She developed a fever this morning and her PMD told her to go to the ED. She has a history of nephrolithiasis requiring ureteroscopy 2 years ago.

PMH: as above

PSH: as above

Allergies: NKDA **Medications:** none

SH: (-) tob; (-) ETOH
FH: (-)
ROS: (-) except for above

PE:

Vitals: T 102.6 P 140 BP 80/40 O2 96% on RA
General: severe distress
Abdomen: soft, right upper quadrant guarding
Back: R CVAT

Labs:

UA → pH 6.5; TNTC WBC/HPF; 2–3 RBC/HPF; (+) bacteria; (-) crystals
CBC → WBC 22 K/μL
Chem 7 → Cr 1.3 mg/dL, CO2 18 meq/L
UCx → pending
BCx → pending

Imaging:
KUB → 2.5 cm radiopaque calculus in (L) upper quadrant
CT scan → 2.5 cm radiopaque calculus in the (L) proximal ureter with partial ureteral obstruction and mild hydronephrosis; normal appearing contralateral kidney

What is your assessment and initial step in management?

46-year-old F with (R) flank pain and likely sepsis 2/2 urinary tract source.

Differential diagnosis includes renal or ureteral calculus, renal tumor, pyelonephritis, papillary necrosis, or some other obstructive process in the collecting system.

You need to stabilize her with IVF and begin empiric antibiotics after sending off appropriate cultures.

After she is stabilized, KUB reveals a 2.5 cm radiopaque calculus in the right upper quadrant and a non-contrast CT shows a 2.5 cm right UPJ stone with marked hydronephrosis.

What do you recommend?

She needs a percutaneous nephrostomy tube.

Right percutaneous nephrostomy tube is placed and the hydronephrosis resolves. She defervesces and becomes stable. Urine culture grows out greater than 100,000 colonies of E. coli that is pansensitive. Blood culture is negative.

She is discharged to home on appropriate antibiotics and returns to see you 6 weeks later. She wants to know what you are going to do for her.

How do you proceed?

The best treatment for this patient is PCNL. See CASES 2 and 5 for further discussion of PCNL.

She undergoes a successful tubeless PCNL. A stent is placed at the conclusion of the procedure. The stent is removed in the office a few weeks later. Stone analysis reveals a calcium oxalate dihydrate stone.

The patient requests a 24-hour urine analysis. It reveals hypercalciuria.

What is the definition of hypercalciuria?

An excretion of urinary calcium exceeding 200 mg in a 24-hour collection.

What are potential causes of hypercalcemia of stone disease?

1. Hyperparathyroidism
2. Sarcoidosis
3. Hyperthyroidism
4. Multiple myeloma
5. Paget's disease
6. Milk alkali syndrome
7. Immobilization
8. Vitamin D intoxication

What are different types of hypercalciuria and their incidence?

1. Absorptive	50–60%
2. Resorptive	4–5%
3. Renal leak	10%

What is the pathophysiology and treatment of absorptive hypercalciuria?

The basic abnormality in absorptive hypercalciuria is intestinal hyperabsorption of calcium. The exact cause of this hyperabsorption is not known.

The resulting increase in the circulating concentration of calcium enhances the renal filtered load and suppresses parathyroid function. Hypercalciuria results from the combination of increased filtered load and reduced renal tubular reabsorption caused by parathyroid suppression. The excessive renal loss of calcium compensates for high intestinal absorption from the intestinal tract and helps to maintain serum calcium in the normal range.

1. Type I: Hypercalciuria occurs during low calcium intake. This is the most common form of absorptive hypercalciuria
    a. Treatment:
        i. Adequate hydration → increase urine volume to > 2 liter (2 quarts)/day

        ii. Low oxalate diet → avoid tea, nuts, leafy green vegetables
        iii. Thiazides → side effect is K$^+$ and citrate depletion
        iv. Sodium cellulose phosphate → a resin that binds calcium; side effects include Mg^{++} depletion and diarrhea

2. Type II: Hypercalciuria occurs only during high calcium intake and usually does not require medical therapy
3. Type III: Hypercalciuria occurs as a result of phosphate leak through the kidney; phosphate loss causes increased calcium absorption from the gut. There is an inverse relationship between calcium and phosphate levels
    a. Treatment:
        i. Adequate hydration → increase urine volume to > 2 liter (2 quarts)/day
        ii. Orthophosphates → inhibit vitamin D production

What is the pathophysiology and treatment of resorptive hypercalciuria?

Resorptive hypercalciuria is increased serum calcium levels due to increased bone demineralization secondary to hyperparathyroidism. Intestinal absorption is frequently elevated because of parathyroid-dependent stimulation of the renal synthesis of 1,25 vitamin D.

These effects increase the circulating concentration and renal filtered load of calcium, often causing significant hypercalciuria. Abnormally high levels of parathyroid hormone enhance renal reabsorption of calcium and phosphate excretion. Similar to renal hypercalciuria, fasting urinary calcium levels are elevated.

Treatment:

Adequate hydration → increase urine volume to > 2 liter (2 quarts)/day
Surgery → parathyroidectomy

How do you treat crisis of hypercalcemia?

Hypercalcemic crisis is treated with hydration, Furosemide, Bisphosphonates and dialysis as necessary.

What are the pathophysiology and treatment of renal leak hypercalciuria?

Renal leak hypercalciuria occurs as a result of impaired tubular reabsorption of calcium. The resulting reduction in serum calcium concentration stimulates parathyroid function.

There may be excessive mobilization of calcium from bone and enhanced intestinal absorption of calcium because of parathyroid hormone excess and ensuing stimulation of the renal synthesis of 1,25 di-hydroxide vitamin D.

These effects increase the circulating concentration and renal filtered load of calcium, often causing significant hypercalciuria. Unlike primary hyperparathyroidism, serum calcium is normal.

Treatment:

Adequate hydration → increase urine volume to > 2 liter (2 quarts)/day
Thiazides → side effect is K$^+$ and citrate depletion

Note: Hypokalemia may be treated with Amiloride (potassium sparing diuretic) or potassium supplements. Hypocitraturia may be treated with potassium citrate.

Name 2 types of hyperoxaluria.

1. Primary hyperoxaluria
    a. This is congenital illness caused by excessive production of oxalate. It results in bilateral nephrocalcinosis and renal failure
    b. There is no effective therapy except for liver transplantation
    c. Most patients die before age of 30 years
2. Acquired hyperoxaluria
    a. This is present in certain enteric diseases:
        i. Inflammatory bowel disease
        ii. Gastrointestinal bypass
        iii. Short gut syndrome

What is the pathophysiology of calcium oxalate stone formation in acquired hyperoxaluria?

Rapid intestinal transit or a diseased terminal ileum results in an increased free fatty acid (FFA) content within the GI system. FFA binds to calcium. Because calcium becomes bound to FFA, calcium is prevented from binding to oxalate. This results in increased absorption of free oxalate and subsequent urinary excretion.

How do you treat calculi associated with hyperoxaluria?

Adequate hydration → increase urine volume to > 2 liter (2 quarts)/day
Low oxalate diet → avoid chocolate, nuts, tea, coffee, spinach, and beets
Low fat diet → avoid fatty meals
Cholestyramine → binds to free fatty acids
Calcium → binds free oxalate

3 years later, she presents to the emergency room complaining of fever, recurrent right flank pain, nausea, and vomiting. A KUB shows no evidence of stone and a non-contrast CT scan shows right hydronephrosis without evidence of a stone. The proximal ureter is not dilated.

What is your differential diagnosis?

Primary or secondary UPJ obstruction, intrinsic or extrinsic mass obstructing the proximal ureter.

What is your next step in evaluation?

Obtain IVP or a CT scan without and with contrast to assess the anatomy of the collecting system and ureters. Make sure that she has not developed a contrast allergy in the interval and check a serum creatinine level.

IVP: prompt excretion of contrast bilaterally. (R) hydronephrosis without evidence of stones or mass; renal pelvis is dilated and there is narrowing of the UPJ. Contrast barely makes it past the obstruction.

What do you do now?

Obtain a Lasix renal scan.

Nuclear renal scan was done and it revealed T½ of 30 minutes in (R) kidney.
T½ was 10 minutes in (L) kidney.

Discuss reference ranges for Lasix nuclear renal scan.

T½	< 12 min	non-obstructed
T½	12–20 min	non-diagnostic
T½	> 20 min	obstructed

What is your clinical assessment of this patient?

Ureteropelvic junction obstruction (UPJ obstruction).

How do you make the diagnosis of UPJ obstruction?

1. Clinical history (patients may complain of symptoms at the time of increased diuresis)
2. Lasix renal scan

What is your initial step in her therapy?

Cystoscopy with retrograde pyelogram and insertion of JJ stent as a temporizing measure. If stent cannot be placed, she needs a percutaneous nephrostomy tube placed.

What are the treatment options for UPJ obstruction?

Treatment options include open or laparoscopic pyeloplasty, retrograde balloon incision (Acucise), ureteroscopic incision with Holmium laser and endopyelotomy.

Your partner recommends percutaneous endopyelotomy.

What precautions should be taken?

Need to ensure there is not a crossing vessel present that you may cut into.

Where do you incise the ureter?

Incision should be performed postero-laterally.

She undergoes percutaneous endopyelotomy and does well from surgery.

CHAPTER 10

FEMALE UROLOGY

UWAIS B. ZAID, MD
NIKKI P. LE, MD

CASE 1

HPI: 23-year-old Caucasian female is referred for urinary frequency and suprapubic pain. She denies gross hematuria. The bladder pain has improved with voiding. There is no flank pain. She endorses urinary urgency and discomfort, which progressively worsens until she voids. She typically wakes 2–3 times per night having to urinate. She denies urinary incontinence. She has been treated for multiple urinary tract infections although these have not been culture proven. Her urinary symptoms worsen with consumption of orange juice, coffee, strawberries, and pineapples.

PMH: Fibromyalgia; irritable bowel syndrome

PSH: none

Allergies: Penicillins (rash); Sulfa (face swelling); Vicodin (nausea)

Medications: Ativan

SH: (+) tob, 1–2 cigarettes/day;
(+) ETOH, drinks 1–2 beers/day; drinks 1 coffee/morning

PE:

Vitals	T 98.8	BP 110/58	P 64	BMI 23
Gen	slightly anxious; tearful when describing symptoms			
Abd	soft, NTND; no scars; no SP tenderness			
GU	normal external genitalia; normal sensation; no prolapse; no foreign bodies; well estrogenized and with normal rugae; examination with mild tenderness at the bilateral levator ani muscles; rectal exam with tenderness at levator ani bilaterally			

Labs

UA	→	pH 6.5, sp gravity 1.01, normal glucose, neg LE, neg Nit, 0 RBC/HPF, 3–5 WBC/HPF
Urine culture	→	negative

What is your assessment and differential diagnosis?

23-year-old CF with LUTs and pain improved with urination. Worsened by acidic foods. The most likely diagnosis is IC/PBS.

Differential diagnosis:

1. IC/PBS
2. UTI
3. OAB
4. Bladder cancer
5. Endometriosis

What treatment options would you recommend?

Per AUA guidelines:

1. First line therapy should include education about normal bladder function, teaching about IC/PBS. Encourage self-care, stress management and coping techniques
    - For this patient recommend dietary modifications: eliminate coffee and exacerbating foods; eliminate/decrease alcohol; smoking cessation
2. Second line therapies include manual physical therapy and multimodal pain management. Oral therapies include Amitriptyline, Cimetidine, Hydroxyzine, or Pentosan polysulfate. Intravesical therapies include DMSO, Heparin, or Lidocaine and may be administered as second-line intravesical treatments

You refer the patient to see a pelvic physical therapist and she starts therapy. She has eliminated acidic foods, smoking, and alcohol from her diet. She still drinks 1 cup of coffee in the morning. You also start oral Pentosan polysulfate (Elmiron). Following these interventions, she has a great response with improvement of her symptoms.

The patient is lost to follow up; however, she returns 10 years later. Her IC/PBS symptoms are well controlled with dietary modifications. She is no longer taking Pentosan polysulfate or seeing the pelvic physical therapist.

In the interim, she has had 2 children both via vaginal delivery. The second required forceps for delivery. She now complains of pelvic pressure and a sense of incomplete bladder emptying. She also endorses incomplete bowel evacuation as well. She denies constipation and urinary incontinence. She does not wear any pads.

What is your next step?

1. Physical examination with POP-Q
2. Labs including urine analysis and possible urine culture

What is the reference point for the POP-Q?

Hymen

What does Aa, Ap, C, TVL represent?

Aa: anterior vaginal wall, 3 cm proximal to hymen. Range is -3 to +3
Ap: posterior vaginal wall, 3 cm proximal to hymen. Range is -3 to +3
C: most distal edge of cervix or vaginal cuff scar
TVL: total vaginal length

Which point cannot be measured with a hysterectomy?

D (measured from posterior fornix).

On examination, normal external genitalia. Sensation intact. Well estrogenized tissue. POP Q measurements:

Aa/Ba/C: +3/+3.5/+4.5
Gh/Pb/TVL: 6/3/10
Ap/Bp/D: +3/+2/+4

What additional maneuvers are necessary for this exam?

Need to reduce the anterior prolapse to determine if any stress incontinence.

With reduction of the prolapse, the patient demonstrates leakage of urine with coughing.

What is your assessment?

23-year-old G2P2 with anterior, apical, and posterior compartment prolapse. Reduction of the anterior prolapse unmasks occult stress urinary incontinence. She also has symptoms of posterior compartment prolapse with stool trapping.

What are options for management of stress urinary incontinence?

Per AUA incontinence guidelines:

Midurethral slings, pubovaginal slings and retropubic suspensions (open or laparoscopic). May consider injection of urethral bulking agents.

Slings can be synthetic, autologous fascia, or cadaveric fascia.

What is the AUA statement on the use of mesh slings for SUI?

The AUA Guideline for SUI concluded that synthetic slings are an appropriate treatment for females with stress incontinence, with similar efficacy but less morbidity than conventional non-mesh sling techniques.

What are contraindications to the use of synthetic slings?

Patients with a concurrent urethrovaginal fistula, urethral erosion, intraoperative urethral injury and/or urethral diverticulum.

How do you counsel this patient on the use of mesh for prolapse repair?

1. The AUA position statement on this topic states that incorporation of mesh into surgical POP repair has potential advantages and disadvantages
   a. Mesh may improve long-term anatomic results of surgery as compared to non-mesh repairs for some types of prolapse; however, better data are needed to determine the appropriate role of vaginal mesh techniques in the treatment of POP
2. Vaginal mesh for POP is associated with risks, including vaginal extrusion, erosion, sexual dysfunction, urinary tract injury, pain and other complications
3. Thorough informed consent should be conducted prior to the use of mesh products for pelvic organ prolapse
4. Surgeons using mesh should:
   a. Undergo rigorous training in the principles of pelvic anatomy and pelvic surgery
   b. Be properly trained in specific mesh implantation techniques
   c. Recognize and manage complications associated with vaginal mesh

What are treatment options for this patient?

1. Open, laparoscopic, or robotic sacrocolpopexy with concomitant or delayed urinary incontinence surgery
2. Transvaginal compartment repair with concomitant or delayed urinary incontinence surgery

The patient elects to proceed with robotic assisted sacrocolpopexy with transobturator synthetic midurethral sling. Intraoperatively during passage of the trocar you perform cystoscopy to evaluate sling placement.

On cystoscopy if you see the trocar traversing the bladder, what is the most likely location in the bladder this would happen?

Most likely on the lateral walls of the bladder.

How do you manage this?

Since a bladder injury, can repass the trocar. Do not need to abandon case.

On cystoscopy what if you see trocar traversing the midurethra and how do you manage?

Given urethral injury, abort placement of sling. Leave Foley catheter in place to allow urethra to heal.

Intraoperative cystoscopy shows some erythema at the left lateral aspect of the bladder. There is no exposed mesh in the bladder. The urethra is patent without any mesh. You place the midurethral sling. The patient has an uneventful recovery and does well with resolution of her prolapse symptoms. She is voiding well with no leakage of urine.

She returns in 1 year for a follow up appointment. In the interim she has had 3 documented urinary tract infections with enterococcus, Klebsiella, and E. coli. She endorses dysuria, urinary urgency, and frequency. Urine analysis shows 50 RBC/HPF, 20–30 WBC/HPF. (-) Nit, (+) LE.

What is your next step?

Cystoscopy, urine culture, and consider upper tract imaging.

1. Urine culture has mixed flora
2. CT scan shows no hydronephrosis or nephrolithiasis
3. There is a calcification in the bladder
4. Cystoscopy shows an area of erythema and edema along the inferior left lateral wall, far from the left ureteral orifice
5. There is a 1 cm calcification attached to the left lateral wall in a non-dependent area. You nudge this with your scope and this reveals exposed mesh

What are your treatment options?

1. Transabdominal mesh excision ± tissue interposition
2. Transurethral laser ablation of exposed mesh or endoscopic excision
3. Transvaginal mesh excision, depending on how high along the lateral bladder wall ± tissue interposition

Patient prefers transvaginal mesh excision with cystolitholapaxy and endoscopic excision of intraluminal mesh. Martius flap is interposed between the bladder and vaginal wall to prevent vesicovaginal fistula formation.

She is followed closely and no longer has significant issues with recurrent UTI’s or bladder calcification.

CASE 2

HPI: 63-year-old Caucasian female presents with urinary frequency and urgency. She has a 6-month history of voiding every 1–2 hours. She wakes 2–3 times/night to urinate. She wears 3 pads/day that are not soaked when changed. Leakage is associated with walking to the bathroom and standing up. She also has leakage while sleeping. She denies leakage with coughing or laughing. She denies gross hematuria and recent urinary tract infections. No dysuria or suprapubic/flank pain. She drinks 2–3 cups of coffee during the day and usually 6–8, 8oz glasses of water during the day. She will have 1 glass of wine with dinner. She went through menopause at age 43 and is not on hormonal supplementation. G1P1, vaginal delivery, atraumatic.

PMH: HTN; HLD; asthma

PSH: Cholecystectomy

ALL: NKDA **Medications**: Lipitor, Lisinopril, Aspirin

SH: (-) tob; (+) ETOH

PE:

Vitals	T 97.7 P 74 BP 164/86 O2 99% BMI 33
Gen	in NAD
Neuro	sensation intact; reflexes symmetric bilaterally; normal ROM and strength
Abdomen	soft, NTND; lap incisions c/w cholecystectomy; no large palpable bladder
GU	atrophic vaginal tissue; normal sensation and strength; no urethral hypermobility; negative cough stress test; no foreign bodies or TTP; no organ prolapse; there is a 5 mm urethral caruncle, non-tender to palpation

PVR is 20 cc, voiding volume 200 cc

Labs:

UA → shows 5 RBC/HPF, neg LE/Nit
UCx → negative

What is on differential?

1. OAB
2. DM
3. Polydipsia can only be evaluated with frequency volume chart
4. Diabetes insipidus (DI) also is associated with frequent, large volume voids and should be distinguished from OAB
5. Interstitial cystitis/bladder pain syndrome shares the symptoms OAB, IC patients have bladder and pelvic pain, including dyspareunia
6. Atrophic vaginitis: in postmenopausal female patient, AV can be a contributing factor to incontinence symptoms. May improve with vaginal estrogen
7. UTI
8. Bladder cancer
9. Bladder stones

What is your next step in workup/management?

Cystoscopy with upper tract imaging (CT Urogram, MR Urogram, Renal Bladder US with RPG) given RBC/HPF.

Cystoscopy shows no bladder tumors, stones, diverticuli. Upper tract imaging shows no filling defects in the renal pelves or ureters and no renal masses.

Are there additional diagnostic interventions you would like performed?

Urodynamics should not be used in the initial workup of the uncomplicated patient.

What non-invasive tool can be used to better characterize urinary complaints?

Voiding diary and pad weight test.

Bladder Diary	
# Daytime voids / volume	6–7/800 mL
# Night time voids / volume	3–4/1000 mL
Total 24-hour voided volume	1800 mL
Avg voided volume	125 mL
Max bladder capacity	400 mL
# UUI episodes	3
# SUI episodes	None

Pad weight:

Number of pads: 2
Weight: 150 grams

What does her nighttime voided volume suggest?

Given nighttime voided volume is 56% of total voided volume, patient has nocturnal polyuria. Evaluate for CHF, renal disease, and consider referral for OSA evaluation.

What is differential diagnosis of nocturnal polyuria?

1. Nocturnal polyuria—production of greater than 33% of total 24-hour urine output during the period of sleep
2. Sleep disturbances (OSA), renal disease, CHF, night time fluid intake, use of diuretics just prior to bedtime

When further queried, the patient endorses snoring and witnessed apneic episodes by her husband. The patient is evaluated by a sleep specialist and diagnosed with OSA.
She is started on a regimen of night time CPAP. With this she only wakes once/night.
A repeat voiding diary shows continued 4–5 low volume leaks during the day associated with going from sitting to standing and walking to the bathroom.

A repeat void diary is performed and shows:

Bladder Diary	
# Daytime voids / volume	9–10/1650 mL
# Night time voids / volume	1/150 mL
Total 24-hour voided volume	1800 mL
Avg voided volume	150 mL
Max bladder capacity	400 mL
# UUI episodes	3
# SUI episodes	None

What is your next line of therapy and how would you proceed with treatment?

1. For all, the initial management includes:
   a. Patient education about urinary tract function, what is known about OAB, benefits versus risks of the available treatment alternatives, and that acceptable symptom control may require trials of multiple therapeutic options before it is achieved
   b. Establish treatment goals with patients
   c. Stress that no treatment is an acceptable choice
2. First line
   a. Offer behavioral therapies (e.g., bladder training, bladder control strategies, pelvic floor muscle training, fluid management)
   b. May be combined with pharmacologic management

The patient continues to have symptoms despite timed voiding, stopping coffee and caffeinated beverage intake, and pelvic muscle floor training.

What additional therapies are available?

Second line therapies per AUA guidelines include oral anti-muscarinics or oral ß3-adrenoceptor agonists. Extended formulations are preferred over immediate release (if available) because of lower rates of dry mouth.

Consider OTC transdermal Oxybutynin patch. If inadequate symptom control and/or unacceptable adverse drug events with one anti-muscarinic medication, then a dose modification or a different anti-muscarinic medication or ß3-adrenoceptor agonist may be tried.

What are side effects of, and contraindications to, anticholinergic medications?

Side effects: dry mouth, constipation, dry eyes, blurred vision, dyspepsia, urinary retention, UTI and impaired cognitive function; rarely, life threatening arrhythmias.

Contraindications: narrow-angle glaucoma unless approved by ophthalmologist; use with extreme caution in patients with impaired gastric emptying and history of urinary retention (may need to CIC).

You start the patient on Oxybutynin XL. She notes a marked improvement in her urinary frequency and is able to postpone voids for 3–4 hours during the day.

She no longer has urinary incontinence episodes. She still wears 1 shield/day for protection; however, this rarely gets wet. She is often able to get through the night without waking up.

You see her in the office and repeat a PVR, which is 30 cc with a voided volume of 250 cc. She is happy with her urination. However, she is complaining of significant constipation and dry mouth that started after the Oxybutynin.

How do you counsel this patient regarding medication therapy?

Per AUA guidelines, before abandoning a therapy that is working, try to manage side effects. For constipation, the guidelines recommend a fiber based stool regimen. For dry mouth, consider oral lubricants, avoiding mouthwashes with alcohol, small sips of water, sugar-free hard candies, and sugar-free gum.

The patient now returns to you 5 years later after being lost to follow up. In the interim, she had initially done well with the Oxybutynin X but noted return of symptoms. Her local physician attempted Tolterodine, Oxytrol, and Mirabegron without response and re-referred her to you due to continued symptoms.

Is there additional workup you would like?

1. UA/UCx
2. PVR
3. May consider urodynamics given recalcitrant symptoms
4. Repeat voiding diary and pad weights.

The patient's UA is normal and UCx with mixed flora, likely contamination. PVR is 50 cc with a voided volume of 150 cc. Urodynamics show a first sensation of 50 cc with uninhibited contractions noted at 85 cc and urge incontinence at 150 cc. Compliance is normal.

Bladder Diary	
# Daytime voids / volume	9–10/1700mL
# Night time voids / volume	2/200 mL
Total 24 hour voided volume	1900 mL
Avg voided volume	150 mL
Max bladder capacity	300 mL
# UUI episodes	3–4
# SUI episodes	None

Pad weight:

4 pads
200 grams

In the interim she is still compliant with her OSA treatment. She has also developed a shoulder rotator cuff injury requiring surveillance MRIs.

What additional therapies do you recommend?

Per AUA guidelines, third line therapies include:

1. May offer intra detrusor OnabotulinumtoxinA. The patient must be able and willing to return for frequent post-void residual evaluation and able and willing to perform self-catheterization for urinary retention if necessary
2. May offer peripheral tibial nerve stimulation (PTNS)
3. May offer sacral neuromodulation (SNS)

What is a contraindication to sacral neuromodulation in this patient's case?

Need for MRIs due to rotator cuff injury.

What are contraindications to OnabotulinumtoxinA (Botox) injection and what are the risks?

Contraindications—pregnancy, breast feeding, neuromuscular compromise (myasthenia gravis, ALS), active UTI

Risks—UTI, urinary retention, focal/generalized weakness

What is the percentage of urinary retention afterwards?

Patients must be willing to CIC in case they develop urinary retention since per AUA/SUFU guidelines there is a 0–43% risk of retention and need for CIC.

How would you dose Botox?

100 units—idiopathic detrusor overactivity
200 units—neurogenic detrusor overactivity

The patient elects to proceed with bladder Botox therapy. You inject 100 units into the bladder and she tolerates the procedure well. She has a great response to the bladder Botox with improved urge incontinence and frequency.

When do you plan to see her back for follow up Botox injection?

The length is variable but typically consider 6 months. If symptoms return earlier, can schedule sooner, or if continued benefits at 6 months, can push out further.

What do you assess at follow up?

Need to check PVR and to ask about UTI symptoms and urinary symptoms.

What do you do if the patient is unable to urinate after Botox injection?

Start a CIC regimen.

Following Botox therapy, the patient has a great response with low residual volumes.

CASE 3

HPI: 54-year-old African-American female presents in clinic for urinary incontinence. The patient underwent a laparoscopic abdominal hysterectomy for enlarged fibroids about 6 weeks prior to presentation. The case was marked by significant EBL; however, she recovered fine initially. She has noted urinary incontinence following the procedure and wears 6–8 large pads/day that are soaked when she changes them. She denies gross hematuria, fevers, nausea, vomiting. She denies flank and suprapubic pain.

PMH: Uterine fibroids, asthma. G2P2, vaginal deliveries without trauma

PSH: Laparoscopic hysterectomy

Allergies: none **Medications:** none

SH: (-) tob; (+) ETOH, occasional drink

PE:

Vitals	T 97.7	P 70	BP 124/62	O2 99%
Gen	in NAD			
Abdomen	healing laparoscopic incisions; no hernias; no palpable bladder			
GU	there is pool of urine in vagina; at the apex, able to palpate area of defect; visual examination shows area of edema and leakage of urine			

Labs:

UA → 5–10 RBC/HPF, 20–30 WBC/HPF, (-) Nit, (+) LE
UCx → mixed flora, likely contamination. Serum Cr 0.9

What additional history about her incontinence would you like?

Is the leakage continuous leakage, associated with straining/coughing/laughing, any OAB symptoms (urgency, frequency, nocturia and urge incontinence).

The leakage is continuous. There is associated urinary urgency. She leaks with coughing and sneezing as well.

What additional interventions would you like?

1. Given RBC/HPF, would recommend upper tract imaging and cystoscopy. (CT Urogram, MR Urogram, Renal Bladder US with RPG)
2. Given continuous leakage, can consider cystogram to evaluate bladder
3. May consider double dye test/blue tampon test

CT Urogram is performed which shows no hydronephrosis, upper tract filling defects.
The ureters opacify all the way to the bladder with no dilation.
Cystoscopy shows a 1.2 cm defect at the mid trigone not involving the ureteral orifices.
There is surrounding edema.
There is leakage of irrigant into the vagina with cystoscopy.

What is your assessment?

54-year-old AAF status post laparoscopic hysterectomy now with a vesicovaginal fistula at the trigone of the bladder.

What is the most common cause of this condition in developing countries?

Traumatic obstructed child birth.

What is the most common cause of this condition in developed countries?

Iatrogenic injuries:

1. 0.1–4% injury rate during pelvic operations
2. Injury to GU tract during hysterectomy (60–75%), hysterectomy for malignant etiology (30%), C section (6%)

What are considerations prior to repair?

1. Diagnose and treat any underlying infections and rule out neoplasms/foreign bodies
2. Ensure appropriate bladder size and function
3. Identification of fistula tract and adjacent structures
4. Optimize patient nutrition and overall health

What are the repair options?

1. Conservative management—more ideal for fistula <3mm for tracts that have not epithelialized. Foley catheter drainage
2. Surgery

For surgery, what is optimal timing?

In uninfected system can do within 2 weeks. Otherwise wait 8 weeks.

What are the surgical approaches?

Transvaginal versus transabdominal.

Describe the steps for repair.

1. Identify and intubate the fistula tract
    a. Wide dissection of the bladder from the vagina
    b. Use healthy, viable tissue for reapproximation
    c. Close fistula with absorbable suture and a second perpendicular imbricating layer of pubocervical fascia
2. Advance a segment of vaginal epithelium past the fistula that provides a third layer and avoid overlapping suture lines
3. An interposition flap can be incorporated, such as martius flap

In high risk cases, including failure or radiated patients, may consider urinary diversion, especially if limited bladder capacity, loss of continence mechanism, or multiple failed repairs.

What are interposition flap options?

1. Peritoneal flap
2. Martius flap—posterior blood supply via posterior labial artery from internal pudendal artery
3. Rectus muscle flap

The patient undergoes a transvaginal repair with Martius flap. She recovers well with resolution of leakage.

CHAPTER 11

VOIDING DYSFUNCTION

BILAL CHUGHTAI, MD
JULIA HAN, MD
DOMINIQUE THOMAS, BS
LAWRENCE YEUNG, MD

CASE 1

HPI: 59-year-old Caucasian male presents with new onset urinary incontinence. The patient complains that his urinary incontinence over the past several months has worsened over the last week after taking cold medicine. His symptoms include hesitating, urinary dribbling and leaking without warning. He currently is using 4–6 pads every day. His most recent PSA was 2 days ago and the results were 5.6 ng/mL.

PMH: NIDDM
BPH

PSH: none

Allergies: none **Medications:** Glyburide, Benadryl PRN

FH: kidney stones
SH: (-) tob; (-) ETOH; postal worker
ROS: non-contributory

PE:

Vitals	T 98.6 BP 180/100 P 90 RR 12
GA	WDWN CM in moderate distress
HEENT	benign
Heart	RRR
Lungs	CTA
Abdomen	soft; NT/ND; palpable suprapubic mass up to umbilicus
Flank	(-) CVAT
GU	normal phallus; adequate meatus; testicles WNL
Rectal	prostate smooth and benign @ 40 g; (-) nodules
Ext	(-) CCE
Neuro	non-focal

Labs

UA	→	patient unable to void
UCx	→	patient unable to void
CBC	→	WNL
Chem 7	→	Na 135 meq/L; K 4.4 meq/L; Cl 100 meq/L; CO_2 18 meq/L; BUN 30 mg/dL; Cr 4.3 mg/dL

What diagnostic tests do you order?

Non-invasive uroflow and post-void residual urine and bladder ultrasound.

Results

Voided urine: patient unable to void
PVR: 2500 mL

What is your next step?

Patient has acute urinary retention; place a urethral catheter.

Do you think his PSA level of 5.6 ng/mL is accurate?

No. His PSA may be falsely elevated due to his urinary retention.

Next step for his PSA?

You need to repeat his PSA after his urinary retention has been treated.

What is your next step?

Renal ultrasound.

Results

Renal ultrasound: (B) hydronephrosis with dilated ureters

At catheterization, 2500 mL of clear urine is obtained, and he still has brisk urine output after 2 hours.

What are your recommendations for this patient?

1. Admit to the hospital
2. Obtain renal ultrasound in 48 hours with Foley catheter in place
3. Obtain vital signs Q 1 hr and check orthostatic blood pressures
4. Follow daily serum electrolytes
5. Check I's and O's, daily weights
6. Check urine for electrolytes
7. Check for urine and serum osmolality

Define post-obstructive diuresis.

By definition, urine output > 200 mL/hr is post-obstructive diuresis.
Post-obstructive diuresis is physiologic diuresis and is usually self-limiting.
Starting intravenous fluids in an awake, conscious patient merely serves to perpetuate the diuresis. Thus, intravenous fluids are usually not required. However, if urine osmolality is greater than serum osmolality, then consider rare salt losing nephropathy.

When does post-obstructive diuresis occur?

Post-obstructive diuresis is a physiological phenomenon that occurs after resolution of bilateral ureteral obstruction or chronic obstruction of a solitary kidney.

How do you manage post-obstructive diuresis?

If patient is awake and alert, place 2 pitchers of water at bedside and allow patient to drink ad lib. If patient is unable to drink, need to give maintenance fluids with D5 ½ NS plus replace urine output ½ cc per cc with D5 ½ NS.

What is your next step in his management?

After he has stabilized and his electrolytes have normalized, discharge him home with an indwelling catheter on clean intermittent catheterization (CIC). Start him on an α-blocker and 5-α-reductase inhibitor. Schedule urodynamic studies as an outpatient in 3–4 weeks.

At 4-week follow-up, he is still performing CIC and is voiding minimal amounts between catheterizations. An interim history as well as the physical exam is otherwise non-contributory.

What diagnostic tests do you order?

Chem 7 → WNL
PSA → 0.8 ng/mL

Urodynamic test results:

Non-invasive Uroflow:		
	Qmax	4 cc/s
	Voided urine	50 mL
	PVR:	500 mL
Filling cystometrogram (CMG):		
	Sensation	normal
	(-) Detrusor overactivity	normal
	Bladder capacity	550 mL
	Compliance	normal
Voiding CMG (Pressure-flow):		
	Qmax	3 cc/s
	Pdet Qmax	85 cm H_2O
	Voided urine	50 mL
	PVR:	500 mL
EMG:		(-) detrusor sphincter dyssynergia

What is your interpretation of the urodynamic findings?

1. High detrusor pressure (Pdet max), low flow system (Qmax)
2. Normal bladder capacity and compliance

What are your treatment options?

1. α-1a-antagonist
    a. α-1a-antagonist combined with clean intermittent catheterization is a reasonable initial option
    b. Relaxes smooth muscle in prostate fibromuscular stroma
    c. Maximal response observed 1–2 weeks
    d. Side effect: orthostasis, nasal congestion, retrograde ejaculation, intraoperative floppy iris syndrome (mainly for tamsulosin)
2. 5α-reductase inhibitor
    a. It will take approximately 6–12 months to achieve a decrease in prostate volume by 20–25%
    b. Will decrease PSA by 50%
    c. Clinical effects observed mainly in men with enlarged prostates (e.g. >40 cc)
3. Combination therapy
    a. Medical Therapy of Prostate Symptoms (MTOPS) trial—showed that combination of α-blocker and 5α-reductase inhibitor prevents progression of BPH better than either agent alone
4. Surgical debulking with transurethral resection of the prostate (TURP)/laser prostatectomy
    a. Since this patient is still in moderate retention after one month of bladder rest, his best option is a bladder outlet procedure. However, you should offer him a trial of α-blockers first
    b. Be prepared to discuss potential risks of TURP
        i. TUR Syndrome
        ii. Obturator reflex
        iii. Perforation of prostatic capsule
        iv. Undermining the trigone
        v. Impotence
        vi. Incontinence
        vii. Bladder neck contracture

CASE 2

HPI: 72-year-old Caucasian male underwent prior radical retropubic prostatectomy 3 years ago for intermediate risk prostate cancer. He reports persistent urine leakage that has increased with coughing or standing; however, he believes he leaks at all times, even when he is lying in bed. He uses 3–5 thick diapers per day. He tried pelvic floor rehabilitation therapy in the past without improvement. He denies hematuria or urinary tract infections. AUA symptom score 20, notable for frequency, nocturia, straining, and intermittency.

PMH: DM type 2; hypertension; gastroesophageal reflux; coronary artery disease; erectile dysfunction

PSH: radical retropubic prostatectomy; right total knee replacement

Allergies: NKDA **Medications:** Metformin, Lisinopril, Omeprazole, Metoprolol, Simvastatin

SH: (+) tob, remote 20-pack year history, quit 30 years ago, (-) ETOH
ROS: negative except for positives in HPI

PE:

Vitals:	stable
General:	NAD
Abdomen:	soft; non-tender; well healed prior low abdominal incision; no hernias; no distension
Extremities:	no peripheral edema
Neuro:	non-focal
GU:	+ circumcised; no lesions to penile shaft or skin, patent urethral meatus at normal position; bilateral descended testicles no masses; + diaper that is soaked; intact perineal sensation; no hernias; normal scrotal skin
DRE:	normal anorectal tone; prostate fossa surgically empty

Labs:

CBC → WBC 6.5; HCT 40%; PLT 425
BMP → Cr 1.2 (baseline)
HgA1c → 7
PSA → <0.01

UA negative for blood or infection
PVR 20 cc

What is your differential diagnosis?

Stress urinary incontinence, urge incontinence, mixed incontinence, overflow incontinence.

Need to be concerned about urinary tract infection, urethral stricture, and bladder neck contracture as the underlying cause.

What additional tests would you order to begin your evaluation?

1. Additional tests
    a. Need to define the extent of urinary leakage and degree of subjective bother to the patient along with desire for treatment. Objective assessment of incontinence can be made with voiding diary and pad weight test
    b. Voiding diary: taking note of daytime and nighttime frequency of micturition, voided volumes, 24-hour fluid input and urinary output and incontinence episodes
    c. 24-hour pad test: highest accuracy of quantification of urine volume. While 24-hour pad test seems most reliable and is recommended by the International Continence Society, 1-hour pad test is more convenient in clinical setting and widely used. 1-hour pad test grading is as follows:
        i. Grade 1: <10 g
        ii. Grade 2: 11 to 50 g
        iii. Grade 3: 51 to 100 g
        iv. Grade 4: >100 g
2. Additional physical exam findings
    a. Physical exam is performed with emphasis on the neurological evaluation assessing the S2–S4 spinal segments, including anal sphincter tone, perineal sensation in the S2–S4 segments, and bulbocavernosus reflex
    b. Standing cough test to evaluate for stress urinary incontinence—have patient stand and cough vigorously with a urinal under penis

Patient returns for a follow-up visit in 4 weeks. Voiding diary shows frequent small volume voids with an average of 5 to 8 episodes of leakage a day associated mostly with activity, coughing, and sneezing. He notes episodes of leakage while lying down. Not associated with urgency. He uses about 3 to 5 thick pads per day; 1-hour pad weight test shows 150 g. Patient is very bothered and strongly desires treatment.

How would you rate his incontinence?

Severe according to his pad test.

What is the next step in management?

Arrange for cystourethroscopy to assess urethral integrity and function and to rule out urethral or anastomotic strictures as well as bladder pathology.

1. Unrecognized urethral and bladder neck pathology can complicate surgery
2. For patients with mild to moderate SUI who are potential candidates for a sling, evaluate degree of residual degree of external sphincter function. Have patient contract pelvic floor while directly visualizing external sphincter activity
3. Paralyzed sphincter may correlate with lower success rates after sling placement

Cystourethroscopy done in clinic shows about a 12 French bladder neck contracture (BNC)

What is your next step?

Begin by addressing the BNC.

When does BNC occur?

1. Usually within 6 months after radical prostatectomy or TURP
2. Patients usually report a gradual decrease in urinary flow

What are risk factors for BNC after prostatectomy?

1. Diabetes mellitus, tobacco use, coronary artery disease, obesity, surgeon expertise, and post-operative complications, such as hemorrhage, prolonged urine leak, and anastomotic disruption
2. Prevention of post-prostatectomy BNC is best achieved through creation of a watertight seal and a tension-free anastomosis with good mucosal apposition

What are the treatment options for bladder neck contracture?

1. Dilation of BNC
    a. Success rates depend on severity of BNC, reported success rates up to 60%
2. Endoscopic incision
    a. Variety of techniques, including cold-knife, electrocautery, laser, hot-knife, and loop resection
    b. Possible higher risk of SUI from sphincter injury after endoscopic incision in comparison to bladder neck dilation.

Are there any special considerations when doing transurethral incision of bladder neck (TUIBN) after radical prostatectomy?

1. After prostatic resection the posterior bladder neck is closer to the rectum, therefore a 6 o'clock incision can injure the rectum
2. Recommend making incisions at 3, 9, and 12 o'clock to avoid rectal injury
3. Catheter usually left in place for 3 to 7 days

What is the latency period following BNC treatment prior to a surgical intervention to treat SUI?

1. Consider period of at least roughly 2 months to assess bladder neck patency prior to AUS implantation to reduce the risk of restenosis and need for further bladder neck manipulation after AUS cuff placement
2. No strict consensus on time of delay prior to AUS placement. Some report 4 to 6 weeks, others as long as 12 months

You dilate the BNC to 24 Fr successfully in the OR and place an indwelling Foley catheter that will be removed in 7 days. He returns in 7 days and passes his voiding trial after Foley catheter removal.

After addressing the BNC, you bring patient back for cystoscopy in 3 months and find that the bladder neck is now widely patent. Very poor residual function of the external sphincter is noted. No abnormal bladder pathology. You also had him redo his voiding diary in the interim. He has greater than 40 episodes of leakage in 4 days, and a 1-hour-pad weight study shows 200g. He notes very frequent urination with small volume voids.

Why would pressure-flow urodynamics be helpful in this patient?

1. Urodynamics should not be included in the basic evaluation of post-prostatectomy incontinence. However, the International Continence Society considers it a useful tool before invasive therapy
    a. Provides assessment of bladder capacity, compliance, and contractility. It can also be helpful when differentiating SUI from overactive bladder symptoms if that is unclear after the basic evaluation
    b. Must also rule out reduced bladder compliance because prolonged storage at high pressures may lead to deteriorating renal function

2. Detrusor hypocontractility may indicate that an AUS is preferable to a midurethral sling because there may not be enough adequate detrusor function to overcome the fixed resistance of a compressive sling
    a. Although 40% to 45% of men with urinary incontinence post-RP have bladder dysfunction, it is usually not the sole cause of incontinence

What is the most common cause of SUI in a male?

Intrinsic sphincter deficiency.

Perform multichannel urodynamic study.

Non-invasive uroflow and PVR:	
Flow curve	normal
Q max	9 cc/s
Voided volume	300 cc
PVR	30 cc
Filling CMG:	
Detrusor instability	none
Bladder capacity	500 cc
Compliance	34 cc/H_20 (normal)
Leak Point Pressure:	
Abdominal (ALPP)	36 cm^2 H_20
DLPP	not seen
Pressure-flow:	
Qmax	12 cc/s
Voided volume	300 (normal)
PVR	30 cc (normal)
Pdet @ Qmax	40 cm H_20 (normal)

Urodynamic findings show:

1. Normal bladder capacity
2. Good compliance
3. Stress urinary incontinence
4. No bladder outlet obstruction
5. Adequate contractility
6. No detrusor instability

Given the information seen on the urodynamics and his voiding diary, what is your recommendation?

Patient continues to have persistent post-prostatectomy urinary incontinence in the late postoperative period (>1 year after surgery) with reduced quality of life, therefore treatment is aimed at a long-term solution.

AUS is treatment of choice for persistent moderate to severe SUI. Success rates 70–80% are dry and 85–95% are dry or improved.

Is this patient a candidate for a male sling?

1. This patient has severe SUI and lacks adequate residual function of his urethral sphincter on cystourethroscopy, therefore a male sling would be less likely to be effective
2. Slings are an alternative for men with persistent SUI with the best results in those with mild to moderate SUI without a prior history of radiation

3. Multiple sling systems are available; no individual recommendations are available to indicate that one sling is superior to another
4. Approximately 55–80% will become dry and 25% are improved but not dry

Is this patient a candidate for transurethral bulking agents?

1. Not likely to be successful due to his severe SUI
    a. Due to the severity of incontinence and postsurgical scarring in the vesicourethral region after his prostatectomy, surgical correction would be first-line treatment
2. Early failure rate is high at 50% and initial success in continence decreases with time
3. Repeated injections needed for satisfactory results
4. Due to the lack of evidence-based data and published low success rates, bulking agents should only be used in highly selected patients with mild SUI, such as the elderly or those with multiple medical comorbidities precluding a more invasive procedure

After discussing potential treatment options with their associated risks and benefits, the patient opts to undergo AUS placement.

Discuss your surgical technique:

The Operation (Insertion of AMS 800)

1. Dorsal lithotomy
2. Midline perineal incision for cuff placement
    a. Measure the urethral circumference
    b. Cuff size of 4.0 or 4.5 cm is generally used for bulbar placement
    c. Optimal site for cuff placement is at the crura just proximal to separating the corporal bodies
3. Inguinal incision for pressure reservoir
    a. Pressure of 61 to 70 cm water pressure reservoir is generally used for bulbar urethra
    b. Fill with 23 cc of an isotonic contrast agent
4. Connect the tubing
    a. Trim the length, use suture-less connectors
5. Cycle the sphincter
6. Perform urethroscopy to assess the function of the sphincter
    a. Closed cuff should show good coaptation
    b. Open cuff should demonstrate sufficient opening for voiding
7. Lock the cuff in an open position

What are contraindications to AUS?

1. Impaired cognitive function or impaired manual dexterity
2. Unresolved urethral stricture or bladder outlet obstruction
3. Unresolved detrusor overactivity
4. Existing infection

What are common complications of AUS?

1. Hematoma (most common)
2. Urinary retention
3. Persistent or recurrent incontinence
4. Device malfunction
5. Urethral atrophy

6. Cuff erosion
7. Infection

Intraoperatively there is a small urethral injury, how would that be managed?

1. If the injury is small it can be repaired with absorbable suture, and if the repair is satisfactory, one can continue with the AUS implant and place the cuff around a different segment of urethra not involved in the urethral injury and repair
    a. Usually a Foley catheter is left in place for about 1 week. However, for purposes of the oral examination, you should choose the most conservative route and choose to repair injury and abort procedure
2. If the urethral injury is large, the AUS placement should be abandoned and a Foley catheter placed

Patient has uneventful placement of AUS and is discharged to home on POD #1. He is discharged to home with AUS deactivated. He returns to clinic in 6 weeks to have it activated and for teaching. After having it activated, patient calls about 4 weeks later reporting persistent incontinence and perineal pain. You schedule an urgent visit.

What does the workup for this persistent incontinence entail?

With recurrent incontinence after AUS placement, you must differentiate between:

1. Inadvertent deactivation
2. Insufficient urethral compression (oversizing of cuff), mechanical failure with fluid loss, cuff erosion, bladder storage failure, urethral or bladder neck atrophy under the cuff, as well as rare causes such as plugged delay fill resistor or kinked tubing

Given patient's symptoms of pain, you also do a physical exam, obtain labs, and order a PVR. Findings listed below:

PE:

Vitals	T 101	BP 110/50	P 88	RR 18
GU	normal phallus; adequate meatus; swollen scrotum that is very tender			
PVR	300 cc			

Pertinent labs show:

WBC → 17,000
Cr → 1.2 (baseline)
U/A → many WBC; few bacteria; moderate LE; negative nitrite
UCx → > 100K Staphylococcus aureus
BCx → no growth

What is your most likely diagnosis?

1. Infection of AUS and possible erosion
    a. Rate of infection with AUS is 1% to 5% and can occur at any time, but most occur within 2 months post-operatively
    b. Most common organisms are skin pathogens such as Staphylococcus epidermidis and Staphylococcus aureus or urinary flora such as E. coli
2. Lower on the differential would be epididymo-orchitis, perineal cellulitis and Fournier's gangrene

What is your next step?

1. Admit patient for antibiotics and stabilization. Antibiotics should be considered before urinary tract manipulation
2. You scope the patient to evaluate status of sphincter cuff by cystoscopy and note the AUS cuff to be exposed in the lumen of the urethra
3. Obtain informed consent to explant the AUS and order appropriate preoperative labs and perioperative antibiotics. All components of the AUS are removed

How would you manage the urethral erosion injury after explanation of the AUS?

1. Insert a 16-French urethral Foley catheter across urethral erosion site and leave indwelling for 2–4 weeks
   a. For large urethral defects or completely transected urethra, can consider performing primary anastomotic urethroplasty if tissues amenable to this
2. Perform a peri-catheter retrograde urethrogram to confirm urethral integrity before removing the catheter

Patient undergoes successful explanation of all components of the AUS. He has an uneventful post-operative course and is discharged to home with the Foley catheter. He returns to your clinic in 2 weeks and peri-catheter retrograde urethrogram shows no extravasation and Foley catheter is removed for voiding trial. Patient passes voiding trial. He returns in 3 months for follow-up, at which time he discusses possibility of replacing AUS.

Is he a candidate for another AUS?

Reimplantation of an AUS may be considered 3 months after explantation once all infection and inflammation have resolved and urethral patency has been confirmed.

1. Successful reimplantation rates of greater than 80% have been achieved
2. When reimplanting AUS cuff after a prior removal for infection or erosion, the cuff should be placed at a site proximal or distal to the previous site as the prior site should be considered compromised and susceptible to future erosion
   a. Some experts prefer a transcorporeal technique for cuff placement at a distal site to decrease risk of erosion
3. Urethral erosion rate 8.7% in patients who are reimplanted after prior urethral erosion or infection

After discussing risk and benefits, patient opts to undergo reimplantation of AUS. Implantation of AMS 800 is done at a healthy site distal to the prior site of erosion, and the surgery and post-operative course is uneventful. Patient returns 6 weeks later to have AUS activated.

The patient subsequently undergoes interval follow-up and remains continent and does well. About 5 years after his reimplantation, he comes back because his urinary incontinence has returned. He denies any other associated symptoms of fever, pain, hematuria, or urinary tract infections. PSA has remained undetectable. On physical exam he has no signs of infection and is otherwise non-contributory. Urinalysis is negative for infection. He is afebrile with stable vitals and has a benign physical exam.

What is your differential diagnosis?

1. Inadvertent deactivation
2. Insufficient urethral compression (due to urethral sub-cuff atrophy)
3. Mechanical failure with fluid loss
4. Cuff erosion

5. Bladder storage failure
6. Urethral or bladder neck atrophy under the cuff
7. More rare would be a plugged delay fill resistor or kinked tubing

How would you proceed in a step-wise fashion?

1. Cycle the AUS
    a. Evaluate for leakage of fluid or mechanical dysfunction
    b. In the situation of detrusor hyperactivity or cuff erosion, the device will cycle normally
2. Obtain imaging with KUB
    a. If system was filled with isotonic contrast solution, KUB can be done to look for loss of fluid from the system
3. Cystourethroscopy
    a. Cycling the cuff at the time will demonstrate poor coaptation with urethral atrophy or fluid loss from system
    b. Direct visualization allows you to evaluate for erosion

On exam his device cycles well and a KUB demonstrates appropriate filling of the reservoir. On cystourethroscopy you note poor coaptation.

What is your diagnosis?

Likely urethral atrophy, which is the reduction in urethral size that can occur as a result of compression of the spongy tissue that is encircled by the occlusive cuff. Occurs in about 10% of patients and is the most common reason for revision of the AUS.

What are treatment options for urethral atrophy?

1. Options include cuff downsizing, movement of the cuff to a more proximal or distal location where the urethra may be thicker, or placement of a second cuff in tandem
    a. Many opt for downsizing of the cuff (3.5 cm is currently the smallest size available) in the same location. If the existing cuff is already 3.5 cm, then it must be repositioned to a more proximal position when feasible
    b. If the cuff is at its proximal limits, then a distal cuff placement either in tandem or single using a perineal or transscrotal incision is an option. Can also place new single cuff via transcorporal technique
2. Simple replacement of the PRB with a higher-pressure reservoir to overcome urethral atrophy is not recommended due to risk of erosion

How would you proceed?

Offer surgical revision to the patient.

After discussing risks and benefits, patient elects for surgical exploration with revision if feasible.

You obtain operative consent with appropriate ordering of preoperative labs and perioperative antibiotics. Patient's cuff is already 3.5 cm so you reposition a new cuff to a more proximal location.

Would you replace a single component or replace the entire device and why?

The AUS has been in place for over 3 years, and thus the entire device should be replaced to reduce the risk of premature failure of another component.

CASE 3

HPI: 60-year-old African-American male with new onset worsening urinary incontinence. Has had leakage for several months, but the symptoms have continued to worsen. Had prior TURP at 48 years of age. He did well for several years; however, he has had increasing intermittency, weak stream, frequency, and straining to void. He was placed on an α-blocker and 5α-reductase inhibitor with minimal improvement. He denies history of urinary tract infections, hematuria, or prior urethral stricture disease.

PMH: NIDDM × 5 years, LUTS, asthma

PSH: none

Allergies: none

Medications: Albuterol inhaler PR, Metformin, Tamsulosin 0.4 mg daily, Finasteride 5 mg daily

FH: (-) prostate cancer
SH: (+) tob 20 pack year; (+) ETOH socially
ROS: non-contributory

PE:

Vitals	stable
General	NAD
Abdomen	soft; nontender; lower abdomen distended
Extremities	no peripheral edema
Neuro	non-focal
GU	circumcised phallus; no lesions to penile shaft or skin; patent urethral meatus at normal position; bilateral descended testicles; no masses; normal scrotal skin
DRE	normal anorectal tone; prostate estimated size 45 g; negative for induration or nodules

What is on your differential for new onset urinary incontinence in this patient?

Stress urinary incontinence, urge incontinence, mixed incontinence, overflow incontinence, and urinary tract infection.

Are there any additional tests you would order at this time?

1. UA and urine culture to rule out UTI
2. Uroflow and PVR to evaluate for urinary obstruction/urinary retention
3. Basic metabolic panel to evaluate renal function

Patient was only able to void a trace amount. His PVR shows 700 cc even after a second void.

UA is positive for trace leukocytes but otherwise negative.
Labs unremarkable except for Cr elevated to 4.3 mg/dL from baseline of 1.2 mg/dL.

What is your assessment and plan?

1. Patient likely has overflow incontinence
2. Insert a catheter to drain the bladder
3. Order a renal ultrasound to ensure he does not have hydronephrosis, especially since his Cr is elevated

Insertion of 18 Fr coude tipped catheter reveals approximately 700 cc of urine. Some resistance met likely in the prostatic urethra but otherwise catheter was easily passed. Patient's renal ultrasound shows evidence of grade 2 bilateral hydronephrosis with dilated ureters.

How would you treat his overflow incontinence?

1. Immediate treatment is emptying the bladder with a catheter
2. Next determine the cause of overflow incontinence, obstruction versus poor detrusor contractility
   a. Anatomic obstruction can be from either urethral stricture disease or prostatic obstruction
   b. Depending on severity of urethral stricture disease, the patient may require a urethral dilation, internal urethrotomy, or urethroplasty
   c. Prostatic obstruction may be treated in a variety of ways, but TURP remains the "gold standard"
   d. Clean intermittent catheterization is an option for obstruction if an invasive treatment is not an option
3. If due to poor detrusor contractility, it is best treated with clean intermittent catheterization

How would you immediately manage this patient?

Admit as an inpatient to closely monitor his renal function, electrolytes, and vitals. Patient is at risk for post-obstructive diuresis.

What is highest on your differential?

Patient has significantly elevated Cr with demonstrated bilateral hydroureteronephrosis likely from a prostatic obstruction. He has no risk factors for urethral stricture disease such as radiation, genitourinary instrumentation or trauma.

What is post-obstructive diuresis (POD) and how is it diagnosed?

1. POD is a polyuric and natriuretic state after the relief of ureteral obstruction in a solitary kidney, bilateral ureteral obstruction, or bladder outlet obstruction
2. Estimated 0.5% to 52% of patients will experience POD after relief of obstruction
3. POD is a clinical diagnosis based on urine output after decompressing an obstructed bladder or ureter. Urine production exceeding 200 mL per hour for 2 consecutive hours or producing greater than 3 L of urine in 24 hours is diagnostic of POD
   a. Physiologic POD is self-limiting and generally lasts 24 hours
   b. Pathologic POD lasts longer than 48 hours and can be exacerbated with excessive intravenous fluid replacement

How would you manage POD in this patient?

1. Strict monitoring of intake and urinary output, daily weights, and monitor serum electrolytes, specifically magnesium, phosphate, urea, and creatinine levels every 12 hours or more frequently as necessary

2. Collect and send a urine sample for urinary sodium, potassium, and osmolality to determine if it is a salt or urea type of diuresis
    a. Urea diuresis is generally self-limiting, whereas salt diuresis can convert to pathologic POD and requires careful monitoring of serum electrolyte levels and hydration status
    b. Spot urine sodium levels greater than 40 mEq/L suggest renal tubular injury and if prolonged can lead to pathologic POD
3. Fluid balance should be closely monitored and a negative balance should be targeted
    a. Recommended to replace 75% of the previous 1-hour urinary output
    b. Avoid excessive fluid because it can prolong or exacerbate the diuresis
    c. Individuals without cognitive impairment should continue to take hydration orally
    d. For the cognitively impaired or those that cannot keep up with urine output via oral intake, administer intravenous 0.45% normal saline at a rate that replaces each mL of urine output with 1 mL of 0.45% normal saline
    e. In physiologic POD, when euvolemia is reached, the diuresis should resolve. This will be evident by a 24-hour urine production of less than 3 L

Patient is admitted to the hospital with an indwelling Foley catheter due to need to strictly monitor ins and outs. Physiologic POD occurs and resolves with close monitoring and oral hydration. Afterwards, the indwelling Foley is removed and he does CIC. His Cr trends back down to baseline. Repeat renal ultrasound shows resolution of bilateral hydroureteronephrosis. Patient is discharged to home and instructed to continue CIC.

He presents for follow-up 4 weeks later. He has been doing CIC every 6 hours and is voiding small volumes in between. Cystourethroscopy in clinic shows lateral coaptation, median lobe intrusion with a patent bladder neck and no urethral strictures. Bladder urothelium is very trabeculated, but there is no other concerning pathology. BMP is unremarkable and shows stable Cr at 1.1 mg/dL. PSA is 1.2 ng/mL.

Why was it appropriate to obtain the PSA at this follow-up versus earlier in his work up?

PSA should not be obtained during the setting of acute urinary retention since it can be falsely elevated. Of note, patient is on Finasteride which decreases PSA by about 50%.

You discuss your findings with the patient and explain that he has failed medical therapy. He asks if he can undergo another TURP since he did so well for several years.

Would you obtain urodynamics in this patient?

Urodynamic testing is optional. However, it should be evaluated in this patient considering his desire for an invasive procedure and because he is having persistent symptoms despite having a prior TURP.

Multi-channel urodynamics:

Noninvasive uroflow:	
Qmax	5 cc/s
Voided volume	160 cc
PVR	550 cc
Filling CMG:	
Sensation	decreased
Detrusor instability	none

Bladder capacity	715 cc
Compliance	normal
Voiding CMG (Pressure-flow):	
Qmax	3 cc/s (low)
Pdet Qmax	15 cm H_20 (low)
Voided urine	200 cc
PVR	515 cc

EMG: negative for detrusor sphincter dyssynergia

Urodynamics show:

1. Low flow evidenced by low Qmax with detrusor hyporeflexia evidenced by low Pdet Qmax
2. No detrusor instability
3. Large bladder capacity with normal compliance
4. Hyposensitive bladder

Do you think he is a candidate for a TURP?

He may not be an appropriate candidate because of detrusor underactivity since he has myogenic failure possibly caused from chronic overdistension from bladder outlet obstruction.

However, there is some evidence to suggest patients may recover detrusor function after relief of prostatic obstruction. If you proceeded with TURP, you would have to counsel him on the potential need to continue doing CIC.

You discuss the results with the patient and he decides to defer pursuing another TURP at this time. He agrees to continue doing his CIC regimen.

CASE 4

HPI: 52-year-old Caucasian male presents 4 weeks after undergoing a TURP. The surgery went well and he had an uneventful post-operative course. The Foley catheter was removed prior to discharge. He presents today with complaints of urinary frequency, urgency, nocturia, and urge incontinence. Patient had some of these symptoms prior to his TURP but the symptoms seem worse. He denies fevers, chills, flank pain, nausea, vomiting, gross hematuria or dysuria. Pathology from TURP was benign.

PMH: LUTS, hypertension, allergic rhinitis

PSH: TURP, laparoscopic cholecystectomy

Allergies: NKDA **Medications:** Amlodipine, Fluticasone nasal spray

SH: (+) tob, prior 10 pack year, quit 20 years ago; (-) ETOH
ROS: (-) except for positives in HPI

PE:

Vitals	stable
General	NAD
Abdomen	soft; non-tender; not distended
Extremities	no peripheral edema
Neuro	non-focal
GU	circumcised phallus; no lesions to penile shaft or skin; patent urethral meatus at normal position; bilateral descended testicles no masses; normal scrotal skin
DRE	normal anorectal tone; no induration or nodules; estimated 30 g
PVR	30 cc

In the initial office visit after a TURP, in addition to a thorough history and physical exam, what else is essential to perform in a patient that complains of persistent LUTS?

1. Urinalysis and urine culture to rule out a urinary tract infection
2. If there is no UTI, initial management of LUTS post-TURP is observation
    a. Some of the irritative voiding symptoms and urge incontinence can be attributed to detrusor instability secondary to prostatic obstruction, the healing resected prostatic fossa, and/or the irritated urethra post instrumentation

How **would you manage this patient if his urine culture is negative?**

1. Provide reassurance that some of the symptoms are expected and self-limiting
    a. Symptoms may worsen up to 4 to 6 weeks after TURP
    b. Most will improve over an additional 6 to 12 weeks until optimal voiding outcome is achieved
    c. Voiding outcomes are usually durable at the 3-month mark
2. Suggest modifications in lifestyle such as stress reduction, timed voiding, fluid restriction, and dietary adjustments such as removal of bladder irritant

Patient returns 2 months later because he continues to have persistent symptoms of urinary frequency, urgency, nocturia, and urge incontinence. He has tried avoiding bladder irritants and timed voiding. AUA symptom score today is 24. UA today is negative for infection.

What is your next step in management?

1. Period of observation in this patient has failed
2. At this time, it is reasonable to perform a non-invasive uroflow and PVR to help guide management
   a. This will help determine whether symptoms are obstructive, non-obstructive, or indeterminate

Patient's uroflow shows a Qmax of 15 mL/s and a PVR of 30 cc.

What is your impression of the uroflow, PVR and what would be your next step in management?

1. Adequate flow rate and no evidence of retention, therefore his symptoms are non-obstructive
2. Reasonable to begin a 2 to 4 week trial of anticholinergics with appropriate counseling on the side effects
3. In addition to anticholinergics, you may trial α-blockers
4. A newer class of medication are the β-3 adrenoreceptor agonists, which relaxes bladder smooth muscle

Patient is unsure if he wants to start a new medication at this time. He asks if there are other possible treatments other than medications.

What is your response?

For patients that are not interested nor candidates for medications, another option may be pelvic floor exercises (PFE).

PFE may help address LUTS by suppressing detrusor muscle spasms through voluntary contractions of the pelvic floor at the time the patient has the sensation to void. Involuntary voiding is inhibited with repeated contractions of the pelvic floor muscles.

After discussion with the patient, he elects to trial anticholinergics. You prescribe Oxybutynin 5 mg twice daily. Patient subsequently returns in 2 months and reports improvement of symptoms and he is satisfied. AUA symptom score is 6. PVR 40 cc.

What is your next step in management?

Patient has shown improvement and will follow up in 6 months with symptom check, uroflow, PVR, and AUA symptom score.

If the patient had returned with failure of improvement on anticholinergics, what would be your next step in management?

Cystourethroscopy and consideration for urodynamic study.

What would these tests tell you and how would you proceed with management?

Cystoscopy can evaluate for urethral stricture, bladder neck contracture, and residual obstructive tissue.

1. If there is obstruction, can trial α-blockers and consider another TURP
2. If there is no obstruction with poor detrusor function, consider CIC, timed voiding, and double voiding
3. If there is no obstruction with detrusor instability, consider intravesical Botox or sacral nerve stimulation

CASE 5

HPI: 66-year-old African-American male previously underwent brachytherapy with external beam radiation for intermediate risk prostate cancer 5 years ago. His initial PSA dropped from 9 ng/mL to 0.03 ng/mL. He has had no evidence of biochemical recurrence. He complains of air in his urine stream. He has concerns that he is passing stool in his urine over the past month as well as urinary drainage from the rectum. This week he has had several days of nausea accompanied by fevers. Denies flank pain, dysuria, hematuria, constipation, or hematochezia. He denies significant lower urinary tract symptoms.

PMH: intermediate risk prostate cancer treated with brachytherapy and external beam radiation; hypertension; diabetes non-insulin dependent; current smoker

PSH: laparoscopic appendectomy

Allergies: NKDA **Medications:** Lisinopril, Metoprolol, Glyburide

SH: (+) tob, 20 pack year, (+) ETOH, social drinker
ROS: negative except for positives in HPI

What is your differential?

Rectourethral fistula.

Presentation of rectourethral fistula is usually not subtle. Most patients have pneumaturia, fecaluria and/or urorrhea, and some patients have fever, chills and septicemia. The fistula can typically be palpated on rectal examination, and the fistula may be visualized cystoscopically.

In addition to obtaining a thorough history, you plan to do a thorough physical exam.

What aspects of the physical exam will you place emphasis on?

Rectal examination.

On digital rectal exam, a defect or the actual fistula can be palpated in the anterior rectal wall.

What other procedures or imaging studies may you order?

1. Procedures: Cystoscopy—fistula can typically be seen
2. Imaging
   a. If the fistula appears to involve the bladder trigone, an excretory urogram (CT IVP) or retrograde pyelogram may be necessary to evaluate for ureteral involvement
   b. Plain film or CT barium enema
   c. Retrograde urethrogram

You decide to perform a retrograde urethrogram and cystourethroscopy. On retrograde urethrogram, you notice extravasation of contrast posteriorly from the prostatic urethra, and upon direct visualization with cystourethroscopy, you note a 5 mm defect at the apex of the prostatic urethra.

Given this information, what are your next steps?

1. Referral to colorectal surgery for evaluation of fecal diversion
2. Consider urinary drainage with urethral catheter
3. Nutritional evaluation to optimize any surgical outcomes
4. Treat any active urine infection

You consult with a colorectal surgeon to perform a diverting loop ileostomy.

How would fecal diversion be managed if he had an injury to the rectal sphincter?

With an obvious severe injury to the rectal sphincter, divert stool with an end colostomy because it would be anticipated to be permanent.

Was the patient a candidate for immediate surgical fistula closure without proximal fecal diversion?

No, because persistent stool passage by the repair site may lead to re-fistulization from chronic inflammation/infection.

What are major patient characteristics to consider when treating a patient with radiation induced rectourethral fistula?

1. Life expectancy
2. Premorbid urinary and bowel function
3. Continence
4. Local anatomy

Patient's nutrition labs show that he has poor nutrition. You work on improving his nutrition, and repeat evaluation in 2 months shows improvement. Patient has also stopped smoking at your counseling.

You do repeat cystourethroscopy and RUG, and you note that there is still a small fistula in the prostatic urethra.

What is your next step?

It is not surprising that the fistula has not spontaneously healed because of his history of radiation. Assess whether the patient desires further surgeries for repair, if he is medically fit for surgery, and whether his bowel and urinary function will be adequate.

Urinary function may be difficult to assess, even with urodynamics, because of inability to retain urine in the bladder for the study due to the fistula

What surgical approach is required for repairing rectourethral fistula?

Can consider perineal or abdominal approach, depending on how high up the fistula is located. Higher fistulas may be better accessible via an abdominal approach with laparoscopic assistance.

The key to the repair is to buttress the repair by interposition of healthy tissue (such as omentum or gracilis muscle) into the plane between the rectum and urethra after closure of the fistula and repair of the urethra.

1. If future urinary and bowel function is not likely to be adequate, consider cystoprostatectomy with urinary diversion; proctectomy and continue current fecal diversion
2. If future urinary function is not likely to be adequate with likely adequate bowel function, consider cystoprostatectomy with urinary diversion; restoration of bowel function via primary repair or proctectomy and colo-anal pull through
3. If future bowel function is not likely to be adequate with adequate urinary function, consider repair of urethral defect with possible buccal mucosa graft and gracilis interposition; proctectomy and continue current fecal diversion
4. If future urinary and bowel function is likely to be adequate, consider repair of urethral defect with possible buccal mucosa graft with gracilis interposition; restoration of bowel function via primary repair or proctectomy and colo-anal pull through

Patient undergoes repair of urethral defect with buccal mucosa graft and gracilis interposition. Pericatheter RUG 4 weeks later shows no extravasation. Foley catheter is removed.

He then revisits colorectal surgery for reversal of his fecal diversion in 6 months. Barium enema and proctoscopy shows no evidence of a leak or fistula.
You do another cystoscopy and RUG which reveal no signs of a rectourethral fistula.
Colorectal surgery arranges for patient to have reversal of his fecal diversion.

CASE 6

HPI: 60-year-old Caucasian male presents with new onset urinary incontinence 4 weeks after abdominoperineal resection for rectal adenocarcinoma. Post-operatively he had urinary retention and failed his voiding trial. Patient had a Foley catheter for 2 weeks post-operatively until he began spontaneously voiding. He endorses leakage without warning and difficulty voiding. He strains and does Crede maneuver to void and his stream is described as a dribble. He uses 3 pads per day. He does not report leakage with coughing, laughing, or sneezing. Denies hematuria, urinary tract infections, fevers, or pelvic pain. Preoperative AUA symptom score was 15.

PMH: rectal adenocarcinoma; asthma; HTN

PSH: APR; laparoscopic appendectomy

Allergies: none **Medications:** none

FH: (-) prostate cancer
SH: (-) tob; (-) ETOH
ROS: non-contributory

PE:

Vitals	stable
General	no acute distress
HEENT	normal
Lungs	CTA B
Heart	RRR
Abdomen	soft; nontender; nondistended; stoma pink and patent with stool in ostomy appliance
GU	uncircumcised phallus easily retractable foreskin; no lesions on glans or shaft of penis; bilateral descended testicles without masses and not tender to palpation
Ext	no edema
Neuro	non-focal

Labs:

UA → negative for infection or RBC
UCx → negative
CBC → WNL
BMP → WNL
PSA → 2.4 ng/mL

What is your initial work-up?

In this patient with recent pelvic surgery and new onset urinary incontinence, it is important to obtain a PVR to evaluate for urinary retention.

Patient voids 100 cc and PVR shows 700 cc.

What is your differential diagnosis?

Overflow incontinence from urinary retention.

Patient likely has bladder dysfunction following colorectal surgery, which is commonly related to extirpative procedures in the region of the autonomic pelvic plexus.

The 2 procedures with the highest incidence of postoperative bladder dysfunction include abdominoperineal resections (approaching 50%) and low anterior resections (15–25%).

What is your next step?

1. Immediately place a catheter to drain the bladder
2. Obtain a renal ultrasound to evaluate for hydronephrosis

You place a Foley catheter and get return of approximately 700 cc of clear yellow urine. Renal ultrasound shows no hydronephrosis.

What is the next step in treatment for the patient?

CIC is the desired management if the dexterity and condition of the patient will allow.

This insures continued "cycling" of the bladder (intermittent distention and evacuation), which maintains the unique compliance of the bladder and minimizes the chance of bladder contraction around a chronic indwelling catheter.

What if the patient does not have the dexterity to do CIC?

Foley catheter placement or suprapubic tube placement are other options of continuous bladder drainage.

What is the prognosis for this patient?

Most likely will regain the ability to empty the bladder, but it may require up to 6 months to recover.

Patient does CIC as instructed. He returns in 1 month and still reports the inability to void and he is getting about 300 cc when doing CIC every 6 hours.

What is your next step?

If the patient remains unable to void, then evaluate using pressure-flow urodynamic studies at approximately 2 to 3 months postoperatively.

The use of urodynamic testing allows more precise determination of lower urinary tract dysfunction, and the CIC protocol can be adjusted based on the storage pressures and bladder capacity at the time of urodynamic evaluation.

It may take up to 6 months for bladder function to return.

Multi-channel Urodynamics:

Non-invasive uroflow:		
	Qmax	5 cc/s
	Voided urine	150 cc
	PVR	700 cc
Filling CMG:		
	Sensation	decreased
	Detrusor instability	absent
	Bladder capacity	700 cc
	Compliance	normal
Voiding CMG (Pressure-flow):		
	Qmax	4 cc/s
	Pdet @ Qmax	5 cm H_20
EMG:		no detrusor sphincter dyssynergia

Urodynamic findings:

1. Hyposensitive bladder
2. Large bladder capacity
3. Normal compliance
4. Impaired contractility

Based on patient's history and urodynamics study, what is your assessment?

Patient likely had detrusor denervation from his prior APR, which is resulting in impaired contractility of the bladder. The contractions are insufficient to adequately empty the bladder.

What is a serious complication that must be considered?

Although the initial presentation is failure to empty, the most serious complications are abnormalities in urinary storage which may lead to a small capacity, poorly compliant, high-pressure bladder.

Some patients with denervation injury will not regain normal bladder function. The patients may persist with decentralized, noncompliant bladders with high storage pressures which, if left unmanaged, could lead to deleterious changes in the upper urinary tract. Even patients that regain urinary function should be closely monitored for the development of a noncompliant, hostile bladder.

Patient agrees to continue doing CIC. He returns in another 2 months for follow-up. Patient notes that he has stopped doing CIC because he is able to spontaneously void on his own now. You obtain a PVR which still shows elevated PVR to 500 cc.

What is your next step?

1. Recommend resuming CIC
   a. If he has a hypocontractile bladder, he needs CIC long-term
2. Concomitant outlet obstruction may be identified, but in the absence of bladder contractility, it usually does not warrant treatment
   a. Other options in patients unable or unwilling to perform CIC via the urethra include catheterizable stoma formation, non-continent ileovesicostomy, or suprapubic tube urinary diversion. Long-term follow-up of these patients will be necessary
3. In patients with non-obstructive urinary retention, sacral neuromodulation has demonstrated improved bladder function and significant reductions in the rate of retention
   a. This is currently approved in patients with non-neurogenic bladder dysfunction, but studies are ongoing in select patients with neurogenic bladder (i.e., denervation injuries)

CASE 7

HPI: 6-year-old male with spina bifida who presents for urinary incontinence. Level of his myelomeningocele is L5. He has episodes of incontinence with urgency. He uses 6 pads per day. He does not catheterize and voids spontaneously. He has had 3 urinary tract infections in the last 6 months. He is able to ambulate with orthotics. He denies any current dysuria or hematuria.

PMH: as above

PSH: back closure at birth; (L5) myelomeningocele; VP shunt × 2; orthopedic procedure × 2

Allergies: latex **Medications:** none

FH: non-contributory
SH: non-contributory
ROS: negative × 10 systems

PE:

Vitals	T 98.6	BP 100/60	P 90	RR 12
GA	young child NAD; ambulates with orthotics			
HEENT	benign; has VP shunt			
Heart	RRR			
Lungs	CTA			
Abdomen	soft; NT/ND; (-) masses; scar in RUQ from shunt noted			
Flank	(-) CVAT			
Back	lumbosacral midline scar			
GU	normal circumcised phallus, adequate meatus; testicles WNL			
Rectal	↓ tone; abnormal BCR			
Neuro	normal upper extremities; consistent with lumbar lesion; some lower extremity wasting			

Labs

UA → WNL
UCx → WNL
CBC → WNL
Chem 7 → WNL

What diagnostic tests do you order?

Renal-bladder ultrasound, VCUG, Urodynamics, and MRI of spine.

Results

Renal ultrasound:	mild (B) hydronephrosis with thickened bladder wall
VCUG:	(L) grade III reflux; bladder neck is closed; the bladder is small and moderately trabeculated

Urodynamic studies:

Non-invasive uroflow and PVR:	
Qmax	20 cc/s
Voided volume	43 mL
PVR	7 mL
Filling cystometrogram (CMG):	
Sensation (filling, fullness, urge)	early sensation
Uninhibited detrusor contractions	50 cm H_2O (abnormal)
Bladder capacity	60 mL (small)
Compliance	8 mL/cm H_2O (poor)
DLPP	63 cm H_2O at 60 mL (high)
ALPP	(-) stress incontinence
Voiding cystometrogram (Pressure-flow):	
Pdet Qmax	30 cm H_2O (normal)
Qmax	19 cc/s (normal)
Voided volume	43 mL (small)
PVR	7 mL (normal)
Flow pattern	bell-shaped; (-) abdominal straining
EMG:	(-) detrusor sphincter dyssynergia
MRI:	(+) tethered cord

What is your interpretation of the UDS study?

1. Small capacity bladder with intact sensation
2. Poorly compliant bladder
3. Uninhibited detrusor contractions generating 50 cm H_2O pressure
4. High DLPP with VUR
5. No SUI
6. Adequate voiding with synergy of detrusor and sphincter

What is your assessment?

6-year-old M with detrusor hyperreflexia, poor bladder compliance, and VUR.

What is your next step?

MRI showed tethering of the cord, and it should be de-tethered prior to any urologic surgery. Also, UDS and renal ultrasound should be repeated after de-tethering of cord.

What is normal bladder capacity of a 6-year-old child?

Normal bladder capacity = (age + 2) × 30 mL = 240 mL.

What is normal bladder compliance?

Normal bladder compliance = 33 mL/cm H_2O.

What is the significance of his DLPP?

DLPP greater than 40 cm H_2O causes renal damage.

What treatment regimen do you recommend?

1. Clean intermittent catheterization with anticholinergic drug
2. Prophylactic antibiotics for VUR
3. Bowel regimen
4. Regular follow-up with UA, urine Cx, renal US, and serum Cr levels

He fails to follow up. 3 years later, he returns to your office. He has had 4 episodes of pyelonephritis documented on DMSA scan with cortical scarring. Upon repeat evaluation, his reflux persists and hydronephrosis is worse.

What is your impression and plan?

Your impression is that his bladder has become considerably more hostile. This is confirmed by repeat urodynamics.

1. You recommend bladder augmentation and ureteral reimplantation. Simultaneous creation of a continent catheterizable channel (appendicovesicostomy or Mitrofanoff) is often helpful in boys
2. Additionally, you recommend creation of a stoma for Malone antegrade colonic enema (MACE) using excess appendiceal length, Monti ileal segment, cecal flap or cecostomy button helps achieve fecal continence in spina bifida children with constipation

Parents agreed. You obtained informed consent and performed the surgery. He did well.

CASE 8

HPI: 12-year-old male with spina bifida and urinary incontinence. The level of his myelomeningocele is L4. He is able to walk with ankle foot orthotics. He is cooperative, able to articulate well. He has regular bowel movements with the use of daily enemas. He does not have any hematuria, dysuria. Uses 1–2 pads daily. Has periodic leakage, sometimes unaware, never with cough, laugh, or sneeze. Had a previous work up of a renal ultrasound as a newborn that was negative and VCUG with no reflux.

PMH: spina bifida (L4)

PSH: back closure at birth; (L-3) myelomeningocele; VP shunt × 2; orthopedic procedure to foot × 2

Allergies: latex **Medications:** none

FH: (+) spina bifida
SH: non-contributory
ROS: normal intelligence; cooperative and well adjusted; negative × 8 systems.

PE:

Vitals	T 98.6 BP 140/60 P 90 RR 12
General	young child in NAD; ambulates with orthotics
HEENT	benign
Heart	RRR
Lungs	CTA
Abdomen	soft; NT/ND; (-) masses
Back	(-) CVAT; midline lumbar scar
GU	normal circumcised phallus; testicles WNL
Rectal	↓ tone, normal BCR
Ext	atrophic lower extremities
Neuro	L4 sensory level; distal lower extremities areflexic

Labs

UA → WNL
UCx → no growth
CBC → WNL
Chem 7 → WNL; Cr 0.8 mg/dL

What would be your initial work up?

Renal ultrasound, VCUG, UDS.

Renal ultrasound: (L) hydronephrosis with some loss of cortex; normal (R) kidney
VCUG: (L) grade IV/V reflux; bladder neck is open at rest

Urodynamic studies:

Non-invasive uroflow:
Voided volume 120 mL

Uroflow	21 cc/s
PVR	60 mL
Filling CMG:	
Capacity	200 mL (small)
Uninhibited detrusor contractions	30 cm H_2O
Compliance	8 mL/cm H_2O (poor)
DLPP	53 cm H_2O at 60 mL (high)
ALPP	40 cm H_2O (low-ISD)
Voiding CMG:	
Pdet@Qmax	30 cm H_20 (normal)
Qmax	19 cc/s (normal)
Voided volume	130 mL (low)
PVR	70 mL (high)
Flow pattern	normal
EMG:	(-) DSD (detrusor sphincter dyssynergia)
MRI:	(-) tethered cord

Summarize the urodynamic findings.

1. Small capacity, poorly compliant bladder
2. Neurogenic detrusor overactivity generating 30 cm H_2O pressure
3. Stress urinary incontinence
4. Elevated PVR, no DESD

How would you assess his kidney function?

Need to obtain DMSA scan for his VUR/scarring.

DMSA: 65% function on (R); 35% function on (L) with upper and lower pole scarring

How do you treat this?

1. Clean intermittent catheterization with anticholinergic medication
2. Prophylactic antibiotics for vesicoureteral reflux (+/-)

CIC plus anticholinergics improve overall incontinence, but patient now notes worsening stress incontinence.

What are your treatment options?

1. Autoaugmentation with ureteral reimplantation and bladder neck sling
    a. Detrusor myotomy with (L) ureteral reimplantation and bladder neck sling is reasonable choice
    b. However this approach does not always achieve adequate bladder capacity
2. Augmentation enterocystoplasty
    a. Enterocystoplasty using stomach, ileum, or colon may be combined with trans-vesical ureteral reimplantation
    b. A sling may also be used; the sling can be made of autologous fascia lata or cadaveric fascia. Synthetic slings are discouraged in children

    c. Alternatively, Kropp urethral implantation (anterior bladder tube), Leadbetter trigonal tubularization, Tanagho bladder neck tubularization, or artificial urinary sphincter may be used to increase the urethral outlet resistance
3. Continent vesicostomy
    a. Mitrofanoff continent vesicostomy with bladder neck closure or sling is an alternative for patients who are unwilling or unable to catheterize per urethra
    b. May create MACE stoma at the same time

Note: You must treat both the high-pressure bladder and low-resistance urethra. Treating only one component will merely compromise the other.
You must teach the patient CIC before any intervention that can lead to retention.

What are contraindications to continent bladder reconstruction?

1. Poor renal function
2. Inability or unwillingness to catheterize
3. Medical non-compliance/poor follow-up

Discuss potential complications and management of bladder augmentation.

1. Detrusor myotomy
    a. Damage to urothelium during myotomy
        i. Close with absorbable sutures (e.g., 4-0 chromic)
    b. Persistent bladder leak
        i. Continued urethral catheter drainage
    c. Failure rate @ 50% with Snow procedure
2. Augmentation enterocystoplasty
    a. Contractions with incontinence (more common with colon)
        i. Anticholinergic (e.g., Imodium, Ditropan)
    b. Mucus formation
        i. Irrigation with saline or water
    c. Hematuria/dysuria syndrome
        i. With stomach only
        ii. Treat with H2 blockers and bicarbonate irrigation
    d. Stone formation
        i. Prevent with irrigation
        ii. Endoscopic or open extraction of bladder stones
    e. Spontaneous perforation
        i. Risk of peritonitis and death is 5–10% if this occurs
        ii. If patient is not toxic, may attempt catheter drainage first
        iii. Operate based on clinical suspicion since cystogram may be falsely negative
    f. Metabolic acidosis
        i. If colon or stomach used
        ii. Can lead to osteoporosis
        iii. Treat with oral sodium bicarbonate or Na/K citrate
    g. Metabolic alkalosis
        i. If stomach used
        ii. Treat with H2 blockers
    h. Malignancy
        i. Adenocarcinoma of the bowel or TCC of the bladder
        ii. Monitor with annual cytology and cystoscopy beginning 10 years after surgery
        iii. Vitamin B_{12} deficiency
        iv. If terminal ileum used
        v. Can cause pernicious anemia and neuropathy

Discuss potential complications and management of the SUI procedures.

1. Bladder neck sling
   a. Rectal perforation
      i. Close in layers; NPO; rectal dilation; antibiotics
      ii. Place SPT and Foley catheter
   b. Unable to catheterize
      i. Perform cystoscopy
      ii. DVIU or revise the sling
      iii. Continent vesicostomy
   c. Persistent stress incontinence
      i. Revise the sling
      ii. AUS or Kropp procedures are alternatives
2. Kropp/Leadbetter/Tanagho bladder tubularization
   a. Unable to catheterize
      i. Perform cystoscopy
      ii. DVIU or revise the bladder tube
      iii. Continent vesicostomy
3. Artificial urinary sphincter (AMS 800)
   a. Implant infection
      i. Antibiotics and possible device explantation
   b. Urethral erosion
      i. Explant the sphincter
      ii. Re-implant 6 months later
   c. Urethral tissue atrophy
      i. Revise the sphincter with smaller cuff/double cuff or higher pressure balloon reservoir
   d. Mechanical failure
      i. Revise the affected component or all components after 2–3 years

The patient underwent enterocystoplasty, rectus fascial sling, and ureteral reimplant. He had an uncomplicated postoperative course and was discharged to home with an SPT.

How would you follow this patient?

1. Cystogram in 3 weeks to exclude extravasation; if negative, remove SPT
2. Repeat VCUG in 3 months to document resolution of reflux
3. Renal US in 3 months, then annually
4. Annual blood work including Chem 7 (and B_{12} level if ileum used)
5. IVP at 3 months and 1 year

2 years later, he presents to the emergency room complaining of fever, chills, vomiting, and flank pain. He had dysuria, urgency and frequency for 2 days. Also has fevers, lethargy, and abdominal pain. Has had decreased PO intake. Has not been catheterizing regularly. Has trouble catheterizing now.

PE:

Vitals	T 102.5	BP 100/50	P 110	RR 20
GA	young child in distress			
HEENT	PERRL, dry mouth			
Heart	RRR			
Lungs	CTA			
Abdomen	soft; tender suprapubic area; (-) masses			

Back	midline scar; (-) CVAT
GU	normal phallus, adequate meatus; testicles WNL
Rectal	↓ tone, normal BCR

Labs:

UA	→	18–20 RBC/HPF; 15–30 WBC/HPF; TNTC bacteria
UCx	→	> 100,000 E. coli; pansensitive
CBC	→	WBC 12 K/µL; Hgb 12 g/dL
Chem 7	→	WNL; Cr 0.8 mg/dL

Differential diagnosis

1. Urinary retention
2. Spontaneous bladder perforation
3. Severe cystitis

Note: In patients with VPN shunt with lethargy and fever, neurosurgery should be consulted to rule out shunt failure/infection.

Abdominal pain could be due to small bowel obstruction secondary to adhesions.

What is your initial treatment?

Patient should be admitted to the hospital, stabilized with IVF, and given IV antibiotics after sending off the cultures. In addition, place a catheter in the bladder and irrigate out any purulent material that may be present.

Catheter: 200 mL cloudy foul smelling urine

What is your next step?

Obtain renal and bladder US and cystogram (alternatively, contrasted CT scan and CT cystogram) followed by cystoscopy when he is stable.

US:	normal upper tracts; three 4 cm hyperechoic mobile structures with shadowing in the bladder
Cystogram:	(-) extravasation; three 4 cm radiopaque filling defects in the bladder
Cystoscopy:	yellow bladder stones; (-) tumor

What is your assessment?

Now 14-year-old M with multiple bladder calculi.

What is your next step?

State that you would perform an open cystolithotomy versus endoscopic treatment after UTI is fully treated. Obtain an informed consent from his parents, order preoperative labs, and give preoperative antibiotics.

Note: If you are going to perform an endoscopic procedure, you must use suprapubic access. If you perform cystolitholapaxy via urethra, you will jeopardize the sling and make him incontinent. Intact removal of stone may be preferable to endoscopic cystolitholapaxy, which is more likely to leave fragments behind which could lead to further stone formation.

Discuss your surgical technique:

The Operation (Open Cystolithotomy)

1. Prep and drape in usual sterile fashion
2. Place Foley catheter
3. Lower midline incision
4. Place ring retractor for exposure
5. Incise the detrusor
6. Avoid bowel portion of the augmented bladder
7. Remove bladder stones
8. Close incision in anatomic layers
9. Leave SPT, Foley, and drain

He undergoes open cystolithotomy successfully. Stone analysis is performed. Chemical composition of the stone is struvite. You recommend CIC 4× daily and bladder irrigation regimen.

CASE 9

HPI: 21-year-old Caucasian male with history of myelomeningocele who presents with urinary incontinence. His myelomeningocele level is L1. He has incontinence which seems to worsen when he experiences coughing and sneezing. He uses approximately 4 pads per day and 1 during the night. He has fairly good bowel habits. He is cooperative and well adjusted. Currently, he is wheelchair-bound and previous work-up has been normal, though he had been on Oxybutynin but had no improvement of his symptoms. He currently performs CIC. He denies any current dysuria or hematuria.

PMH: myelomeningocele (L1)

PSH: back closure at birth; (L1) myelomeningocele; VP shunt × 2; orthopedic procedure × 2

Allergies: latex **Medications:** none

FH: (+) spina bifida
SH: non-contributory
ROS: normal intelligence; cooperative and well adjusted; (-) seizures; regular BM with laxatives and suppositories

PE:

Vitals	T 98.6	BP 140/60	P 90	RR 12
GA	WDWN CM INAD sitting in a wheelchair			
HEENT	benign			
Heart	RRR			
Lungs	CTA			
Abdomen	soft; NT/ND; (-) masses			
Back	midline scar			
GU	normal phallus; adequate meatus; testicles WNL			
Rectal	↓ tone; abnormal BCR			
Ext	atrophic lower extremities			
Neuro	L1 sensory level; distal lower extremities are hyper reflexes			

Labs

UA → WNL
UCx → no growth
CBC → WNL
Chem 7 → WNL; Cr 0.8 mg/dL

What diagnostic tests do you order?

Renal-bladder ultrasound: US: normal upper tracts, bladder with small amount of urine.

Urodynamics: see results below.

Multichannel urodynamic studies

Non-invasive uroflow and PVR:

Uroflow	18 cc/s
Voided urine	350 mL
PVR	7 mL

Filling CMG:	
IDCs	(-) detrusor hyperreflexia
Capacity	350 mL
Compliance	30 cc/H_2O
Leak Point Pressures:	
DLPP	no leak
ALPP	40 cm H_2O

Summarize the urodynamic findings

1. Normal bladder capacity and compliance
2. Stress incontinence
3. No urge incontinence

What are your treatment options for this patient?

1. Periurethral bulky injection
    a. Success rate with bulking agents is very low
2. Male sling
    a. This is also an option, but he may need CIC after surgery
3. Leadbetter trigonal tubularization
    a. May need CIC
4. Tanagho bladder neck tubularization
    a. May need CIC
5. Kropp anterior bladder tube implantation
    a. May need CIC
6. Artificial urinary sphincter (caution needs revisions q5–7 years)
    a. This is perhaps best option for this patient since he will likely be able to void

Discuss your surgical technique:

The Operation (Insertion of AMS 800)

1. Dorsal lithotomy position
2. Inguinal incision for pressure reservoir
    a. Pressure of 61–70 cm H_2O is generally used for bulbar urethra
3. Perineal incision for cuff placement
    a. Measure the urethral circumference
    b. Cuff size of 4.5 cm is generally used for bulbar placement
4. Connect the tubing
5. Cycle the sphincter
6. Lock the cuff in open position
7. Leave Foley catheter in overnight

The patient underwent placement of AMS 800 artificial urinary sphincter. He had an uncomplicated postoperative course and was discharged to home.

How would you follow this patient?

1. Activate AUS at 6 weeks
2. Document adequate bladder storage with US or catheterization
3. US in 3 months to rule out upper tract deterioration after increasing outlet resistance; repeat yearly
4. Serum Cr yearly

A year later, he comes to the clinic and has complaints of recurrent incontinence and bilateral flank pain. For the past 2 months he has had urinary frequency and urinary incontinence. He has not been able to empty his bladder on a regular basis.

PE:

Vitals	T 98.6	BP 110/50	P 90	RR 18
GA	WDWN CM in wheelchair			
Abdomen	soft; tender suprapubic area; (-) masses			
Back	midline scar; (B) CVAT			
GU	normal phallus; adequate meatus; testicles WNL			
Rectal	↓ tone, normal BCR			

Labs:

UA	→	normal
UCx	→	no growth
CBC	→	WBC 8 K/µL; Hgb 12 g/dL
Chem 7	→	WNL; Cr 1.4 mg/dL

What is your initial treatment?

Patient should be assessed to ensure sphincter is working and deactivate it with a cuff in an open state. The cuff is left open. Next, a catheter will be placed in his bladder to check PVR.

Catheter: 5 mL urine

What is your next step?

Obtain renal US and VCUG.

Renal US:	(B) moderate hydronephrosis with ureterectasis
VCUG:	(-) vesicoureteral reflux; 100 mL bladder capacity with some trabeculation

What is your next step?

Perform multichannel urodynamic studies.

Multichannel urodynamic studies:

Non-invasive uroflow and PVR:	
Uroflow	18 cc/s
Voided urine	100 mL
PVR	7 mL
Filling CMG:	
IDCs	12 cm H_2O
Capacity	100 mL (small)
Compliance	10 cc/H_2O (poor)
Leak Point Pressures:	
DLPP	no leak demonstrated
ALPP	no leak demonstrated

Summarize the urodynamic findings.

1. Small capacity, poorly complaint bladder
2. Detrusor contractions generating 12 cm H_2O pressure

What is your assessment?

Decompensated bladder since increased outlet resistance was created.

What are your treatment options for this patient?

1. Anticholinergic therapy and leave the sphincter open
   a. Reasonable initial therapy
   b. If this fails, proceed with bladder augmentation and sphincter revision
2. Immediate bladder augmentation
   a. Too aggressive at this time but may be required if anticholinergic therapy fails

Patient agreed to anticholinergic therapy and the cuff was left open. 3 months later, he returns to your office complaining of side effects from his anticholinergic medication (by now you have offered him all available pharmacotherapy), and his incontinence is no better. He desperately wants to be dry.

What is your next step?

1. Consider intravesical Botox injections
2. Proceed with bladder augmentation

CASE 10

HPI: 15-year-old Caucasian male with enuresis. He has diurnal incontinence and fecal incontinence as well as occasional urinary incontinence that has never been worked up. He wears 2–3 pads per day for his incontinence. He has nocturia about 2 times a night and during the day he voids 6–8 times. In the past 2 years he has had 2 UTIs. His neurologic history reveals a decrease in deep tendon reflexes. He has no presentation of fever, chills, nausea or vomiting.

PMH: UTI × 2 in past 2 years

PSH: none

Allergies: none **Medications:** none

FH: (-) congenital urological problems (e.g., UPJ, VUR, etc.); (-) siblings
(-) maternal ingestion of drugs
SH: none
ROS: none

PE:

Vitals	T 98.6 BP 140/60 P 90 RR 12
GA	young CM ambulating with abnormal gait
HEENT	benign; (-) VP shunt
Heart	RRR
Lungs	CTA
Abdomen	soft; NT/ND; (-) mass
Back	lumbosacral dimple
GU	normal circumcised phallus; adequate meatus; testicles WNL
Anus	normal anatomic position; abnormal gluteal clefts; palpable coccyx
Rectal	decreased BCR
Ext	high arched feet
Neuro	decreased deep tendon reflexes

Labs

UA → WNL
UCx → WNL
Chem 7 → Cr 0.6 mg/dL
CBC → WNL

What is your differential diagnosis?

15-year-old CM with enuresis and neurologic findings. Differential diagnosis includes tethered cord and spinal dysraphism.

What diagnostic tests do you order?

Renal-bladder ultrasound, KUB, VCUG, Urodynamics, MRI of spine.

Results:

Renal ultrasound: normal
Bladder US: thickened bladder wall
KUB: normal
VCUG: (-) VUR and moderate PVR; "Christmas tree" bladder with multiple bladder diverticula
MRI (L/S spine): tethered cord

Multichannel urodynamic studies:

Non-invasive uroflow and PVR:	
Uroflow	16 cc/s
Voided Volume	80 mL
PVR	0 mL
Filling CMG:	
Capacity	80 mL (small)
IDC	15 cm H_2O (abnormal)
Compliance	6 mL/cm H_2O (poor)
Leak Point Pressure:	
DLPP	50 cm H_2O (high)
VLPP	normal
EMG:	(-) detrusor sphincter dyssynergia

Summarize the urodynamic findings

1. Poorly compliant, small capacity bladder
2. No stress incontinence
3. No detrusor sphincter dyssynergia

What is your assessment?

15-year-old CM with newly diagnosed tethered cord with small capacity, overactive bladder without stress incontinence.

What are the treatment options for this patient?

1. Anticholinergic therapy
2. Timed voiding
3. Bowel regimen
4. Clean intermittent catheterization
5. Neurosurgery consult for cord de-tethering

What does DLPP > 40 cm H_2O signify?

Persistently elevated DLPP will lead to upper tract deterioration.

What are other treatment options if cord de-tethering does not work?

If medical therapy fails after cord de-tethering, he will need bladder augmentation.

Either autoaugmentation or enterocystoplasty may be performed. Autoaugmentation may not provide adequate bladder volume. With enterocystoplasty, he may not empty well and may need to perform CIC.

Consider continent catheterizable channel in ambulatory male.

What is your follow-up?

Continued follow-up with serial Cr and renal-bladder ultrasound as well as urodynamics (as needed) is important.

What is the relationship between tethered cord and bladder dysfunction?

During puberty, the vertebral column lengthens vertically.
When spinal cord is tethered, it becomes stretched under tension.
Spinal cord becomes ischemic when tension is placed on it.
Ischemic spinal cord can produce bladder dysfunction.

How do you treat chronic constipation if conservative measures fail?

MACE (Malone antegrade colonic enema): give enema through the cecum

CASE 11

HPI: 20-year-old Caucasian male with a history of bladder exstrophy managed with ureterosigmoidostomy due to inability to close the bladder as a neonate presents now for recurrent pyelonephritis. He has had 2–3 episodes per year for the last 3–4 years. He denies fevers, chills, nausea, vomiting, back pain, leg weakness, rectal incontinence or bleeding. He denies any history of stones. Additionally, he has not had imaging or scope of his ureterosigmoidostomy since the procedure.

PMH: bladder exstrophy, pyelonephritis

PSH: cystectomy and ureterosigmoidostomy, epispadias repair

Allergies: none **Medications:** none

FH: none
SH: (-) tob; (-) ETOH
ROS: non-contributory

PE:

Vitals	T 98.6 BP 140/60 P 90 RR 12
General	short and thin CM in no acute distress
HEENT	unremarkable
Heart	RRR
Lungs	CTA B
Abdomen	soft, non-tender non-distended; well healed midline surgical incision
Flank	no CVAT
GU	microphallus with evidence of epispadias repair; adequate meatus; bilateral testicles WNL
Rectal	normal sphincter tone; no masses; 15 g smooth prostate
Neuro	non-focal

Labs:

CBC	→	WBC 10 K/μL; Hgb 9 g/dL; HCT 27%
Chem 7	→	Na 138 meq/L; K 3.2 meq/L; Cl 115 meq/L; CO_2 19 meq/L; BUN 15 mg/dL; Cr 1.9 mg/dL
Hemoccult	→	normal

Note: Need to work up his anemia and metabolic acidosis.

How would you evaluate his anemia?

Must determine whether this is microcytic versus macrocytic anemia. His MVC value was low/normal, and reticulocyte count was low.

What does this mean?

His anemia is likely secondary to renal insufficiency from low erythropoietin production.

How do you treat this?

Supplemental iron and addressing renal insufficiency.

What is the most common metabolic abnormality associated with ureterosigmoidostomy?

Hyperchloremic hypokalemic metabolic acidosis.

What are the metabolic consequences of the various urinary diversion procedures?

Bowel Segment	Electrolyte Abnormalities	Acid-Base Disorder	Metabolic Effects	Treatment Options
Stomach	↓Cl- ↓K+	Metabolic alkalosis	B_{12} malabsorption Peptic ulcers Hematuria-dysuria syndrome	Hydration B_{12} supplementation Antacids
Jejunum	↓Na+ ↓Cl- ↑K+	Metabolic acidosis	Dehydration Stimulation of aldosterone secretion	Hydration NaCl, NaHCO3
Ileum & Colon	↓K+ ↑Cl- ↓Ca++ ↓Mg+	Metabolic acidosis	Dehydration B_{12} malabsorption (with ileum)	Hydration Alkali therapy Nicotinic Acid B_{12} supplementation

How do you correct his metabolic acidosis?

Oral chloride restriction, replacement oral alkali therapy with Polycitra, and drainage of the area of storage with rectal tube.

What is your next step?

Recommend imaging of upper tracts.

CT-IVP:	severe L hydronephrosis with thin renal cortex; moderate R hydronephrosis with preservation of renal parenchyma; bilateral ureteral dilation down to level of sigmoid colon at anastomosis on both sides; no calculi

What is your assessment?

Anemia, metabolic acidosis, and hydronephrosis.

What is your differential diagnosis?

1. Chronic ureteral dilation—may be chronic dilation without distal obstruction
2. Ureteral obstruction—may have stricture at the ureterosigmoid anastomosis; also have to rule out adenocarcinoma at the ureterosigmoid anastomosis
3. Vesicoureteral reflux—may have bilateral refluxing ureters

Does he need any additional work up?

He needs a nuclear renal scan to assess for renal function. He also needs a sigmoidoscopy and barium enema to evaluate his sigmoid colon.

1. Renal scan with Lasix
   a. Results:

(R) 80%	T½	30 min
(L) 20%	T½	40 min

   b. No improvement in drainage with colon evacuation
   c. He has high grade bilateral ureteral obstruction

Note: Lasix dose for an adult = 1 mg/kg. Obstructed: T½ > 20 min; Indeterminate: T½ = 15–20 min; Non-obstructed: T½ < 15 min

2. Barium enema: normal
3. Flexible sigmoidoscopy: normal without evidence of tumors

What is your assessment?

Patient with bilateral ureteral obstruction at level of anastomosis to sigmoid colon. This patient needs relief from ureteral obstruction or another urinary diversion to preserve his upper tracts.

What are your options?

1. Bilateral percutaneous nephrostomy tubes
   a. Not a good option due to poor quality of life
2. Percutaneous nephrostomy with balloon dilation
   a. This treatment has low success rate
3. Revise ureterosigmoid anastomoses
4. Different form of urinary diversion
   a. Can consider continent urinary diversion or ileal conduit
   b. At the time of reconstructive surgery, you must remove the cuff of sigmoid and implanted portion of distal ureters

Why do you have to remove the cuff of sigmoid and implanted portion of distal ureters?

They are at risk of developing adenocarcinoma.

What choices do you have for urinary diversion?

1. Ileum is a good choice due to familiarity by urologists
2. Transverse colon is also a good choice, but must perform barium enema and flexible colonoscopy prior to surgery
3. Jejunum is another reasonable alternative; however, must monitor for risk of hyponatremic, hypochloremic, hyperkalemic acidosis

After discussing pros and cons of all options, he agrees to ileal conduit.

What is a contraindication for continent urinary diversion?

Performing continent urinary diversion in setting of renal insufficiency can lead to severe metabolic abnormalities.

How would you prepare this patient?

1. Obtain informed consent by discussing the surgical procedure, indications, potential risks, and complications
2. Obtain all preoperative labs and tests
3. Perform bowel prep patient and place sequential compressive devices (SCDs)
4. Obtain Chem 7, CBC, Coags, CXR, EKG, T&C for 2 units PRBCs, and give prophylactic antibiotics

What are the AUA Antimicrobial Prophylaxis Best Practice Recommendations for open or laparoscopic surgery involving intestine?

Procedure	Organisms	Prophylaxis indicated	Antimicrobials of Choice	Alternatives	Duration of Therapy
Urinary Diversion	GU tract, skin and intestine	In all patients	2nd/3rd generation Cephalosporin Aminoglycoside + Metronidazole or Clindamycin	Ampicillin/ Sulbactam Ticarcillin/ Clavulanate Zosyn Fluoroquinolone	24 hours

Source: Wolf JS Jr., Bennett CJ, Dmochowski RR, et al. Best Practice Policy Statement on Urologic Surgery Antimicrobial Prophylaxis. J Urol 2008;179:1379–90 Table 3a. Copyright© 2008 American Urological Association. Published by Elsevier Inc. Used with permission.

What is your surgical technique for a ileal conduit?

1. Harvest the conduit—stay 15–20 cm proximal to ileocecal valve to maintain bile salt and vitamin B_{12} absorption
2. Perform the ileo-ileal anastomosis and close the mesenteric trap
3. Create Bricker type uretero-ileal anastomosis
4. Place single J stents
5. Create the rosebud stoma

What is your technique to excise the ureterosigmoidostomy?

Remove the cuff of sigmoid, remove implanted portion of distal ureters, then obtain frozen sections.

What is your follow-up?

1. Follow-up on pathology-ischemic fibrosis—no evidence of malignancy
2. Monitor for renal insufficiency and metabolic abnormalities (hyponatremic, hyperchloremic metabolic acidosis)

CHAPTER 12

MALE INFERTILITY

SJIO PAREKATTIL, MD

CASE 1

HPI: 32-year-old Caucasian male who has been unable to conceive with his wife. He has never fathered any children in the past. His wife is 31-years-old and they have been trying unsuccessfully for the past 2 years. They have been having unprotected intercourse every 3–4 days. His wife has undergone an infertility evaluation by her gynecologist and she states that "everything is OK." He has normal potency, libido, and ejaculation. He does not have a history of surgery, chemotherapy, radiation, or heat exposure. He does not have a history of mumps, ETOH, tobacco, viral illness, environmental toxins or chronic illness.

PMH: none

PSH: none

Allergies: none **Medications:** none

FH: none
SH: (-) tob; (-) ETOH
ROS: non-contributory

PE:

Vitals	T 98.6	BP 140/60	P 90	RR 12
GA	WDWN CM INAD			
HEENT	benign			
Heart	RRR			
Lungs	CTA			
Abdomen	soft; NT/ND			
Flank	(-) CVAT			
GU	normal circumcised phallus; adequate meatus; (B) testicle WNL; Grade III (L) varicocele			
Prostate	smooth and benign @ 30 g; (-) nodules or induration			
Ext	(-) CCE			
Neuro	non-focal			

What initial lab tests do you order?

UA → WNL
UCx → no growth
Testosterone → WNL
Semen analysis:

Volume	3.0 mL
Concentration	18 million/mL
Normal motility	40%
Normal morphology	40%
"Stress pattern"	yes

What is the role of endocrine evaluation for assessing male fertility?

Hormonal abnormalities are well recognized, although not common causes of male infertility. Whether to get a baseline testosterone level is controversial.

Good reasons to get a testosterone level are:

1. Abnormal semen analysis, especially if sperm concentration < 10 million/mL
2. Impaired sexual function
3. Suspected endocrinopathy (based on physical exam, for instance)

What does the basic endocrine work-up, i.e., for a low sperm concentration, consist of?

1. S-testosterone
2. FSH

What do you do if you find a low S-testosterone level?

1. Repeat a total and free testosterone
2. LH
3. Prolactin (PRL)

What does a high FSH with normal LH, PRL, and testosterone indicate?

Sign of abnormal spermatogenesis.

Does this patient need to be evaluated for obstruction?

No. Since his semen volume is normal, there is no need to evaluate for obstruction (i.e., semen fructose) or retrograde ejaculation.

Does he need to be evaluated for testicular failure (primary or secondary)?

No. Since he is producing normal sperm, there is no need to evaluate for testicular failure (i.e., testis biopsy).

What is "stress pattern" seen on semen analysis?

Stress pattern consists of low count, poor motility, and poor morphology.
These changes are not pathognomonic of varicocele but represent abnormal testicular function seen in many patients with or without varicoceles.

What are minimally adequate semen parameters (2010 WHO criteria)?

Parameter	Lower reference limit
1. Volume	1.5–5 mL
2. pH	≥ 7.2
3. Concentration	> 15 million/mL
4. Total number of sperm	> 39 million per ejaculate
5. Total motility	> 40%
6. Progressive motility	> 32%
7. Sperm morphology	> 4% normal forms
8. Forward progression	> 2.0 (scale 0–4)

Note: Must obtain at least 2 semen analyses 3 days apart.

What is your assessment?

This patient has oligospermia with normal semen volume as well as left-sided varicocele based on physical exam findings.

What do you do now?

Recommend scrotal US.

Scrotal US: Grade III varicocele of (L) scrotum;
(B) testicles WNL

Note: Scrotal US is optional in this patient as an extension of the physical exam.

When should you obtain transrectal ultrasound (TRUS)?

TRUS should be obtained in an azoospermic patient to rule out ejaculatory duct obstruction.

When should you obtain renal ultrasound?

Obtain renal ultrasound to rule out renal agenesis in the setting of congenital absence of the vas(a) and in a patient with cystic fibrosis.

What is your assessment?

32-year-old CM with oligospermia and Grade III left varicocele.

What is your recommendation?

Recommend left varicose ligation.

How do you proceed?

Obtain informed consent. Potential complications include bleeding, infection, hydrocele formation, recurrence of varicocele, vas transection, and testicular atrophy.

Describe your surgical technique:

The Operation (Inguinal Approach—Ivanissevich)

1. Incise skin over inguinal crease
2. Incise external oblique aponeurosis
3. Avoid ilioinguinal nerve
4. Mobilize the spermatic cord
5. Dissect out the cord and identify dilated spermatic veins
6. Clamp, cut, and ligate veins (usually 3)
7. Preserve the testicular artery
8. Close the incision in layers

The Operation (High Retroperitoneal Approach—Palomo)

1. Incise skin over the site of internal inguinal ring
2. Incise external oblique aponeurosis
3. Split the internal oblique muscle

4. Push the peritoneum medially
5. Clamp, cut, and ligate spermatic veins (usually 3)
6. Preserve the testicular artery
7. Close the incision in layers

The Operation (Subinguinal with Magnification)

1. Make a subinguinal incision
2. Mobilize the cord
3. Ligate all veins
4. Leave 2 or 3 lymphatics
5. Preserve testicular artery
6. Close the incision

Discuss complications and management of varicocele ligation.

1. Ligation of testicular artery
   a. This may result in testicular atrophy but is less likely with retroperitoneal approach
      i. This complication may be avoided by using optical magnification and using vasodilating agents such as papaverine or 0.25% mepivacaine
2. Recurrent varicocele
   a. This may be due to missing 1 of the veins
   b. Alternatively, the varicocele may have been caused by compression of the (L) renal vein by SMA—the "nut-cracker phenomenon"
3. Transection of the vas
   a. Vasal injury is less likely with high retroperitoneal approach
   b. If vas is transected, vasovasostomy should be performed using optical magnification and 9–0 or 10–0 nylon sutures

What is your follow-up?

Repeat semen analysis Q 3 months for 1 year.

After 1 year, he remains oligospermic.

What do you do next?

State that you would reassess the patient, obtaining a complete history, review of system, and physical examination.

No change. The couple has continued to try but without success. The patient's wife is now 33-years-old.

What do you recommend?

Repeat semen analysis × 2.
Results are consistent with oligospermia.

What else do you recommend?

The couple should consider one of the following:

1. Artificial insemination
2. Artificial insemination into uterus after sperm washing
3. In-vitro fertilization with embryo transfer (IVF+ET)
4. Intra-cytoplasmic sperm injection (ICSI)
5. Gamete intrafallopian transfer (GIFT)

The patient and his wife elect to undergo ICSI and ultimately conceive a healthy girl. The patient thanks you for your counseling and guidance.

What is meant by infertility being a "couple" problem?

Both the male and the female are equally responsible.

1.	Female factors	50%
2.	Male factors	50%

What are potential risk factors for infertility?

1. Loss of libido
2. Reduction or loss of accessory glands
3. Cryptorchidism
4. Leydig cell hyperplasia
5. Sertoli cell only
6. Intersex
7. Cystic fibrosis
8. Retrograde ejaculation
9. Anejaculation

How do you evaluate an infertile female?

1. History and physical
2. Hormonal profile
3. Basal body temperature
4. Hysterosalpingogram
5. Post-coital test
6. Laparoscopy

What surgical options are available for an infertile male?

1. Varicocele ligation
2. Transurethral resection of ejaculatory ducts
3. Vasovasostomy
4. Vasoepididymostomy

CASE 2

HPI: 32-year-old Caucasian male who has been unable to conceive with his wife. He has fathered 2 children from a previous relationship. His wife is 29-years-old and they have been trying unsuccessfully for the past 2 years. His wife has undergone an infertility evaluation by her gynecologist and she states that "everything is OK." He has normal potency, libido, and ejaculation. He does not have a history of surgery, chemotherapy, radiation, or heat exposure. He does not have a history of mumps, ETOH, tobacco, viral illness, environmental toxins or chronic illness.

PMH: none

PSH: none

Allergies: none **Medications:** none

FH: cystic fibrosis
SH: (-) tob; (-) ETOH
ROS: non-contributory

PE:

Vitals	T 98.6	BP 140/60	P 90	RR 12
GA	WDWN CM INAD			
HEENT	benign			
Heart	RRR			
Lungs	CTA			
Abdomen	soft; NT/ND			
Flank	(-) CVAT			
GU	normal circumcised phallus; adequate meatus; (B) testicle WNL; (B) vasa palpable			
Rectal	prostate smooth and benign @ 20 g; (-) nodules or induration normal rectal tone; normal BCR			
Neuro	non-focal			

What initial lab tests do you order?

UA → WNL
UCx → no growth

Semen analysis:

Volume	2.8 mL
Concentration	0/mL
Normal motility	N/A
Normal morphology	N/A

T → normal

What is your assessment?

32-year-old CM with azoospermia but normal semen volume.

What is your next step?

Obtain a transrectal ultrasound to visualize the seminal vesicles. Dilated seminal vesicles, dilated ejaculatory ducts, and/or midline prostatic cystic structures are suggestive of complete or partial ejaculatory duct obstruction.

Prostate ultrasound → (-) ejaculatory duct obstruction

How would you correct ejaculatory duct obstruction?

Perform transurethral resection of ejaculatory duct.

Semen volume associated with ejaculatory duct obstruction is usually ≤ 1.0 mL.

What is your differential diagnosis?

1. Primary testicular failure
2. Secondary testicular failure
3. No evidence of obstruction

What do you do now?

Recommend testis biopsy.

How do you proceed?

Obtain informed consent. He agrees and tolerates the procedure well.

What is your follow-up?

Ask for pathology report.

Testis biopsy reveals maturation arrest of both testes.

What is your assessment?

32-year-old CM with azoospermia and maturation arrest.

What is your recommendation?

Recommend artificial insemination with ICSI.

How do you treat infertility due to chronic prostatitis?

Prescribe antibiotics for 6 weeks.

Diagnosed by alkaline pH and leukocytes on semen analysis.

What is a sperm antibody test and when is it indicated?

It is a test that detects antibodies present on spermatozoa surface. There are 2 types of assay—mixed agglutination reaction and the Immunobead assay. The mixed agglutination reaction involves mixing the patient's sperm with RBCs coated with human antibodies.

Antisperm antibodies on the sperm cause linking and agglutination of RBCs. Immunobead assay uses polyacrylamide beads with rabbit antihuman antibodies. These beads bind to sperm containing antisperm antibodies.

Testing for sperm antibodies should be considered in patients with isolated asthenospermia (poorly motile sperm) with normal sperm concentration, sperm agglutination, or an abnormal postcoital test. It can also be performed in other cases of unexplained infertility.

How do you treat infertility due to positive anti-sperm antibodies?

1. Oral steroids
2. Assisted reproduction

What are potential complications of steroid use in infertility?

1. Cataracts
2. Hip necrosis

What is sperm penetration assay (SPA)?

SPA or postcoital test determines sperm's ability to traverse through the cervical mucus.

1. Inhibition of sperm's penetration is called "cervical factor"
2. "Cervical factor" can be induced by progesterone and is seen in women using OCP
3. Cervical mucus becomes clear and thin just prior to ovulation
4. A normal test is defined as one in which more than 10–20 sperm are identified per HPF and majority of sperm should show progressive motility
5. Normally spermatozoa survive in cervical mucus 2–4 days

When is SPA or postcoital test performed?

Postcoital test is performed in cases of hyperviscous semen, unexplained infertility, and low-volume or high-volume semen specimens with good sperm density. It is a microscopic examination of the cervical mucus, performed shortly before expected ovulation and within hours of intercourse, to identify the presence of motile sperm in the mucus.

When should you obtain karyotype?

Obtain karyotype if Klinefelter's Syndrome is suspected (e.g., long arms and legs with small firm testicles).

How do you treat vasal or epididymal obstruction?

1. Vasovasostomy
2. Vasoepididymostomy
3. Epididymal sperm extraction

How do you treat anejaculation?

1. α-agonist
2. Electroejaculation under anesthesia

How do you treat retrograde ejaculation?

1. Extract sperm via urethral catheter
2. α-agonist

How do you retrieve sperm from a urinary bladder?

1. Patient alkalinizes urine with sodium bicarbonate 1 day before collection
2. Empty the bladder with urethral catheter
3. Rinse bladder with Ringer's glucose solution
4. Leave 2 mL in the bladder
5. After masturbation, patient voids or sperm is harvested using a catheter
6. Sperm is concentrated with centrifugation and used for artificial insemination

How do you treat idiopathic hypofertility?

1. Clomiphene citrate
2. hCG and hMG

If no abnormalities are noted in the evaluation, infertility is termed idiopathic.

What is clomiphene citrate?

It is anti-estrogen. Clomiphene blocks estrogen receptors in hypothalamus. This causes increased release of GnRH to stimulate pituitary gland.

Pituitary gland secretes increased FSH and LH. LH causes Leydig cells to produce testosterone and FSH stimulates Sertoli cells. These hormonal changes are hoped to improve sperm production.

Pregnancy rates with clomiphene citrate are lower than 30% in most studies.

Dose: 25–50 mg/day over a 3–6 month period.

What is hCG?

1. Has LH-like activity
2. Stimulates intratesticular production of testosterone
3. 2500–5000 IU IM, 1 to 3 ×/week for 12–15 weeks
4. Insufficient evidence hCG has therapeutic efficacy

What is hMG?

1. Has equal LH and FSH activity
2. Often used in combination with hCG on the theory that added FSH stimulation may improve the success of gonadotropin therapy
3. Insufficient evidence for using hMG in combination with hCG routinely

CASE 3

HPI: 42-year-old African-American male who has been unable to conceive with his wife. He has never fathered any children in the past. His wife is 33-years-old and they have been trying unsuccessfully for the past 18 months. His wife has not undergone an infertility evaluation by her gynecologist. She has delivered 3 children from a previous relationship. He has normal potency, libido, and ejaculation. He does not have a history of surgery, chemotherapy, radiation, or heat exposure. He does not have a history of mumps, ETOH, tobacco, viral illness, environmental toxins or chronic illness.

PMH: none

PSH: (L) inguinal hernia repair; (-) vasectomy

Allergies: none **Medications:** none

FH: none
SH: (-) tob; (-) ETOH
ROS: non-contributory

PE:

Vitals	T 98.6	BP 140/60	P 90	RR 12
GA	WDWN AAM INAD			
HEENT	benign			
Heart	RRR			
Lungs	CTA			
Abdomen	soft; NT/ND; (L) inguinal hernia incision scar			
Flank	(-) CVAT			
GU	normal circumcised phallus; adequate meatus; (L) testicle WNL @ 4 × 3 cm in size; (R) testicle small and atrophic @ 3 × 2 cm in size; (B) vasa palpable; (-) varicoceles			
Rectal	prostate smooth and benign @ 20 g; (-) nodules or induration normal rectal tone; normal BCR			
Neuro	non-focal			

What initial lab tests do you order?

UA → WNL
UCx → no growth
Post-ejaculate urine → (-) sperm seen

Semen analysis:

Volume	0.5 mL
Concentration	0/mL
Normal motility	N/A
Normal morphology	N/A

What is your next step?

Repeat semen analysis with semen fructose.

Semen analysis:

Volume	0.3 mL
Concentration0/ mL	
Normal motility	N/A
Normal morphology	N/A
Semen fructose	(-) fructose

What does fructose negative, low ejaculate volume azoospermia suggest?

It means that seminal vesicle fluid is not present.

What does fructose positive, low ejaculate volume azoospermia suggest?

It suggests retrograde ejaculation, bilateral vasal obstruction or incomplete specimen collection since seminal vesicle secretions are present.

What is your differential diagnosis?

Differential diagnosis includes ejaculatory duct obstruction, primary or secondary testicular failure, bilateral congenital absence of the vas deferens, and ejaculatory dysfunction.

What is your next step in evaluation?

Obtain hormonal tests.

FSH → normal
LH → normal
T → normal
PRL → normal

What is your next step?

Obtain transrectal US to rule out ejaculatory duct obstruction.

TRUS of ejaculatory duct: (-) ejaculatory duct cyst;
(-) seminal vesicle dilation

What is your next step in evaluation?

Obtain scrotal US to rule out other pathology such as epididymal cyst that may be causing mechanical obstruction.

Scrotal US: (R) testis and epididymis are normal. (-) varicoceles
(L) testis and epididymis are normal. (-) varicoceles

What is your assessment?

Azoospermic male with low volume, fructose negative semen.
Patient also has a small atrophic testis.

What do you do now?

Recommend testis biopsy.

How do you proceed?

Obtain informed consent. He agrees to proceed.

Describe your surgical technique:

The Operation (Testicular Biopsy)

1. Use open testicular biopsy method
2. Inject local anesthesia to scrotum
3. Use a "window" technique
4. Make the testicular incision on the medial or lateral surface of the upper pole of the testis
5. Avoid injuring a major end artery located just beneath the tunica albuginea

He tolerates the procedure without complications and is discharged to home.

What is your follow-up?

You need to ask for the pathology report.

Testis biopsy reveals normal spermatogenesis of (L) testis and Sertoli cell only of (R) testis.

What is your assessment?

42-year-old AAM with normal left testicular function.

What is your recommendation?

You recommend left vasogram and reconstruction of the vas at the time of vasogram if obstruction is noted.

How do you proceed?

Obtain informed consent for vasovasotomy and potential vasoepididymostomy.

He agrees to proceed.

The Operation:

(L) vasogram: Obstruction at the (L) inguinal area at previous hernia repair site.

During the vasal reconstruction, you discover that the vas is scarred in place at the inguinal canal. Vasal excision and primary end-to-end vasal anastomosis cannot be performed.

What are your treatment options?

1. Reconstructive surgery
    a. Vasovasostomy
    b. Vasoepididymostomy
2. In-vitro fertilization (IVF)
3. Donor insemination
4. Micromanipulation

What do you do now?

Transect the right vas deferens immediately distal to the proximal convoluted portion of the vas and bring it to the left testis to perform right-to-left vasovasotomy.

The right vas deferens is too short to reach the left vas deferens.

What do you do now?

Bring the right vas deferens through the scrotal septum (via a button-hole you created) to the left hemiscrotum.

The vas is still too short.

What do you do now?

Swing the left testis and move it to the right hemiscrotum.

The left testicle does not reach the right vas deferens.

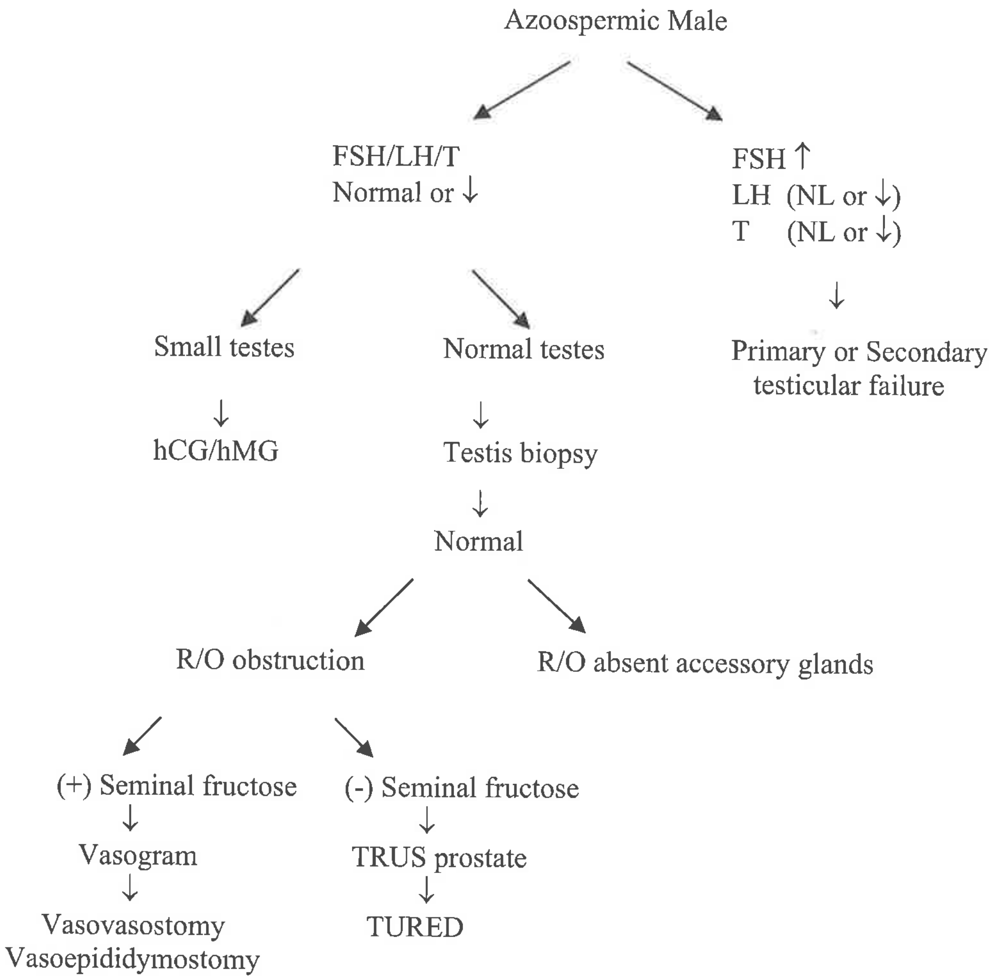
What do you do now?

Mobilize the proximal convoluted portion of the vas deferens and the epididymis of the right testis to gain more vasal length.

This was done and vasovasostomy was completed successfully. He went on to father 3 children.

Discuss the algorithm for evaluation of azoospermic male:

Algorithm for Evaluation of Azoospermic Male:



CASE 4

HPI: 35-year-old Caucasian male who has been unable to conceive with his wife. He has never fathered any children. They have been having unprotected intercourse twice per week. His wife is 29-years-old and they have been trying unsuccessfully for the past 3 years. His wife has undergone an infertility evaluation by her gynecologist, which was reportedly normal. She has never been pregnant before. He has normal potency, libido, and ejaculation. He does not have a history of surgery, chemotherapy, radiation, or heat exposure. He does not have a history of mumps, ETOH, tobacco, viral illness, environmental toxins or chronic illness.

PMH: none

PSH: none

Allergies: none **Medications:** none

FH: cystic fibrosis
SH: (-) tob; (-) ETOH
ROS: non-contributory

PE:

Vitals	T 98.6	BP 140/60	P 90	RR 12
GA	WDWN CM INAD			
HEENT	benign			
Heart	RRR			
Lungs	CTA			
Abdomen	soft; NT/ND			
Flank	(-) CVAT			
GU	normal circumcised phallus; adequate meatus; (B) testicle WNL; (B) vasa non-palpable			
Rectal	prostate smooth and benign @ 20 g; (-) nodules or induration normal rectal tone; normal BCR			
Neuro	non-focal			

What initial lab tests do you order?

UA → WNL
UCx → no growth
Testosterone → WNL
Semen analysis:
  Volume 2.0 mL
  No sperm seen

What is your next step?

State that you would obtain a semen fructose level and sweat test.

Semen fructose → WNL
Sweat test → Positive

What do you do now?

Hormone tests are unnecessary in this patient since his bilateral testicles are normal in size and consistency. However, the most important finding in this patient is that his vasa are not palpable. However, if hormonal levels were obtained, they are shown below.

FSH → normal
LH → normal
T → normal
PRL → normal

What imaging studies do you recommend?

Recommend renal US.

Renal US → (L) renal agenesis; (R) kidney normal

Note: Obtain renal US to rule out renal agenesis in the setting of cystic fibrosis.

What is your assessment?

Congenital bilateral absence of vas due to cystic fibrosis.

How do you make the diagnosis of cystic fibrosis?

1. Positive family history
2. Positive sweat test

What is the most accurate method of diagnosing cystic fibrosis?

Positive sweat test is most accurate for diagnosing cystic fibrosis.

What is your next step?

Perform cystic fibrosis screening.

Cystic fibrosis screen revealed Delta F508 mutation.

Note: Congenital bilateral absence of vas is different entity from unilateral absence of vas and renal agenesis. Cystic fibrosis gene encodes a chloride channel.

What is Delta F508 mutation?

Delta F508 mutation is a 3 base-pair deletion in the CF gene.
It represents 70% of mutated alleles.
Delta F508 is a severe mutation that occurs most commonly in cystic fibrosis.

What do you now?

Recommend cystic fibrosis screen on the spouse.

Cystic fibrosis screen is negative.

What is your recommendation?

Recommend artificial insemination with ICSI and testicular sperm extraction.

What is the probability that their offspring will have cystic fibrosis?

1. The offspring will most likely be a carrier since the mother does not have a mutation
2. The male must have 2 mutations in order to have congenital bilateral absence of vas
3. If the mother has a mutation that is not detected by the CF screen, the offspring will have congenital bilateral absence of vas

How is cystic fibrosis transmitted?

1. Autosomal recessive
2. Patients give a positive family history

What is the probability that a North American woman of European descent is a carrier of cystic fibrosis gene?

The probability is 1/25.

Discuss the relationship between cystic fibrosis and alleles.

1. If both alleles have a severe mutation, the patient will manifest pulmonary and pancreatic symptoms
2. If 1 allele has mild mutation and the other has severe mutation, congenital bilateral absence of vas may result
3. If 1 allele is normal and the other has mild mutation, the patient is a carrier

What are clinical manifestations of cystic fibrosis?

1. Respiratory problems
   a. Emphysema
   b. Bronchopneumonia
   c. Bronchiectasis
2. Gastrointestinal problems
   a. Intestinal obstruction
   b. Meconium ileus
3. Male infertility (99% males)
   a. Absent or defective vas deferens
   b. Absent or defective epididymis
   c. Absent or defective seminal vesicles

How do you treat potential complications of cystic fibrosis?

1. Pancreatic insufficiency
   a. Pancreatin (Viokase)
   b. Pancrelipase (Cotazym)
2. Pulmonary insufficiency
   a. N-acetylcysteine (Mucomyst)

CHAPTER 13

SEXUAL DYSFUNCTION

BOBBY B. NAJARI, MD
JOHN P. MULHALL, MD

CASE 1

HPI: A 65-year-old heterosexual man presents with erectile dysfunction (ED). He is only sexually active with his wife, a 63-year-old woman. They have been married for 38 years and she is not present at the office visit. He has good libido, they are sexually active once a week, and he does not masturbate. He is presenting due to a gradual decline in erectile function over the past 5 years. For the past year, his erections have not been hard enough for penetration. This has become a source of frustration for the couple and his goal is to improve erectile function enough for penetrative sex. He no longer experiences nocturnal or morning erections. His orgasm and ejaculation is normal.

PMH: hypertension; hyperlipidemia; adult onset diabetes mellitus

PSH: none

FH: father died of myocardial infarction at 60
SH: (-) tob; (+) ETOH, 1 drink a day; no illegal substance use; retired bank manager
ROS: no symptoms of prolactinoma and thyroid dysfunction

Allergies: none **Medications:** Lisinopril, Metformin

PE:

Vitals	P 60 BP 170/100
GA	awake and alert; normal masculine hair distribution
Chest	no gynecomastia
Heart	RRR, no murmurs
Lungs	clear
Abdomen	soft; non-tender; non-distended
Genitourinary	normal circumcised phallus; normal meatus; normal firm 16 cc testes bilaterally, no varicocele bilaterally; normal 20 cc prostate
Extremities	intact femoral and pedal pulses

Describe the relevant nerves of the penis.

Sensory—Dorsal nerves of the penis provide sensory feedback via the pudendal nerve.

Sympathetic nerves (T10-L2)—Superior and inferior hypogastric plexus pelvic plexus cavernous nerves. These release norepinephrine, which is involved in maintaining flaccidity and causing detumescence.

Parasympathetic nerves (S2-3)—Pelvic plexus cavernous nerves. These release nitric oxide (NO), the key neurotransmitter for erections.

Describe the physiology of an erection.

Cavernosal artery smooth muscle relaxation is the first step. During stimulation, parasympathetic cavernosal nerves release NO, increasing the production of cGMP, which relaxes the cavernosal smooth muscle.

The arterial dilation allows for increased arterial inflow, allowing expansion of lacunar spaces. This expansion compresses the penile venous outflow, which include the subtunical venules and the emissary veins that traverse the tunica albuginea. Thus, erections are a balance between the inflow and outflow of penile blood.

Detumescence occurs with the release of norepinephrine by sympathetic nerves, which causes vasoconstriction resulting in decreased arterial inflow and increased venous outflow.

What are key components of sexual history?

Personal:	gender identity, sexual orientation, age of sexual partner(s), relationship status, relationship duration, frequency of sexual activity
Sexual dysfunction:	severity, onset, rate of decline, nocturnal erections, ability to sustain erection, exacerbating or alleviating factors, previous treatments, degree of distress, goal of treatment
Social:	job, stress level, life changes, health changes associated with sexual dysfunction timing

What lab tests will you order for this patient?

Recommended:

ED is associated with cardiovascular disease and diabetes mellitus and can be the first symptom of these diseases. Check blood pressure, lipid profile, and fasting serum glucose or HgA1c in all men presenting with ED.

These patients should also be evaluated for testosterone deficiency, most commonly with a morning serum total testosterone. A complete blood count (CBC) and serum chemistry will also evaluate for other causes of ED, such as anemia and renal failure.

Optional:

Testing should be tailored to the patient's complaints and risk factors. Hyperthyroidism can cause ED, so a patient with sign or symptoms suggestive of hyperthyroidism should be screened with thyroid stimulating hormone (TSH), which will be low.

Hyperprolactinemia suppresses GnRH, leading to LH suppression and low testosterone. If a patient has a visual field defect, headaches, gynecomastia, or decreased libido, check a prolactin. Prostate specific antigen (PSA) and digital rectal exam can have significance in men being treated with testosterone replacement therapy; however, in a man presenting with ED, follow the PSA screening guidelines: shared decision-making is the key.

Labs results:

HgA1c → 5.8%
Morning total T: → 430 ng/dL
Lipid panel → normal
PSA → 1.2 ng/mL
CBC → normal
Chem 7 panel → Normal

What is your assessment and differential diagnosis?

ED can be classified as psychogenic, organic, or mixed. Organic causes include vasculogenic (arteriogenic and venoocclusive dysfunction), neurogenic, endocrinologic, and medication induced. This is a 65-year-old man with ED, likely organic, given his comorbidities and family history.

What is the next step in your evaluation?

Prior to treatment for ED, he needs a cardiac risk assessment to evaluate the risk of a mortal or morbid event during or shortly after sexual activity.

Exercise tolerance should be assessed prior to the initiation of therapy in all patients and can help in the assessment of cardiac risk. Per the Princeton Consensus III recommendations, sexual activity is equivalent to walking 1 mile on a flat surface in 20 minutes or briskly climbing 2 flights of stairs in 10 seconds.

All patients with ED, regardless of risk, should be counseled on lifestyle modification, including smoking cessation, regular exercise, weight loss, a healthy diet, and moderate alcohol consumption.

Low-risk patients can be treated for ED without any further evaluation. High-risk patients must be advised to cease sexual activity until cleared by their cardiologist. Intermediate risk patients require further risk evaluation by a stress test before resuming sexual activity.

Cardiovascular risk assessment

Low Risk	Intermediate Risk	High Risk
Successfully vascularized patients (CABG, stent)	Mild to moderate stable angina	Unstable or refractory angina
Left ventricular dysfunction/heart failure (NYHA Class I or II)	Congestive heart failure (NYHA Class III)	Congestive heart failure (NYHA Class IV)
Mild valvular disease		Moderate to severe valvular disease such as aortic stenosis
Asymptomatic controlled hypertension		Uncontrolled hypertension
	Past MI without intervention (2-8 weeks) awaiting evaluation	Recent MI without intervention (<2 weeks)
	Non-cardiac atherosclerotic disease, such as peripheral artery disease, stroke, transient ischemic attacks	High risk arrhythmia, such as exercised induced ventricular tachycardia, poorly controlled atrial fibrillation
		Obstructive hypertrophic cardiomyopathy with severe symptoms

When asked about exercise tolerance, he states he is able to walk 1 mile on a flat surface in under 20 minutes.

How would you counsel this patient?

Given his uncontrolled hypertension, he should be advised to cease sexual activity and see his cardiologist. He should be counseled on lifestyle modification. He should also be advised to bring his partner to the next visit, as treatment for ED is optimized when the patient and the partner are both involved in the shared decision-making process.

The patient sees his cardiologist, and it turns out he was not taking his Lisinopril as prescribed because of a bothersome cough it caused. His cardiologist prescribed Losartan instead, and he returns to you 6 months later with an unchanged presentation except for a blood pressure of 120/60. He is cleared to resume sexual activity and brought his wife.

What are his treatment options? How would you counsel him?

Unless contraindicated, oral pharmacotherapy with Phosphodiesterase type 5 inhibitor (PDE5I) is first line treatment in men with ED. There are four approved PDE5I agents: Sildenafil (Viagra), Tadalafil (Cialis), Vardenafil (Levitra), and Avanafil (Stendra).

There is no evidence to support the superiority of one agent over the others. The choice of drug will depend on details of the patient's sexual history, such as sexual frequency (occasional or multiple times a week) and spontaneity (routine schedule or unpredictable).

Other treatment options include:

1. Intracavernous vasoactive drug injection therapy is the most effective non-surgical treatment for ED. However, it is also more invasive relative to other non-surgical treatments and has the highest potential for priapism
2. Intraurethral prostaglandin E1 (alprostadil) is less effective than intracavernous injections, but it is less invasive and is a reasonable option for men who fail PDE5I or cannot take them
3. Vacuum erectile devices are low-cost treatment options for men with infrequent sexual intercourse or comorbidities requiring non-invasive medication-free management of ED. Low patient acceptability limits its applicability in many patients

What are potential treatment options the patient may inquire about but which are not recommended?

Testosterone therapy is not indicated for the treatment of ED in the patient with a normal serum testosterone. Even if serum testosterone is slightly low, testosterone replacement therapy rarely improves ED if that is the only symptom. This important principle is in the AUA and EAU guidelines, as well as being a point in the AUA Choosing Wisely campaign.

Yohimbine, herbal therapies, and topical therapies to the glans penis or penile shaft are not recommended.

What are the common side effects of PDE5I? What are differences between the side effects of these agents?

Headache (13–16%), facial flushing (4–14%), dyspepsia (4–9%), dizziness (2–5%), nasal congestion (5–12%), visual change (<2–4%).

Sildenafil and Vardenafil have higher affinity for PDE-6, which is located in the retina. These agents are more likely to cause chromatopsia (visual color change) or blurry vision. Myalgia and back pain are more common with Tadalafil (5%).

What are absolute and relative contraindications for the use of PDE-5 inhibitors?

PDE5I potentiate the hypotensive effects of organic nitrates and are absolutely contraindicated in men taking these medications, as well as men using amyl nitrate or amyl nitrite ("poppers") recreationally.

All PDE5I interact to some degree with α-blockers even in healthy volunteers to decrease blood pressure. Patients should be on stable dose of an α-blocker prior to initiating PDE5I.

PDE5I should be started at the lowest dose in these patients and titrated cautiously. Vardenafil may prolong the QT interval, and should be used with caution in patients with a known history of QT prolongation or on drugs with similar side-effects.

What are the pharmacokinetic differences between the available PDE5I? Why is this clinically relevant?

Sildenafil and Vardenafil are similar in that their Tmax is approximately 1 hour and their serum half-life is 4 hours. Tadalafil has a Tmax of 2 hours and a serum half-life of 18 hours. Avanafil has a Tmax of 0.5–0.75 hours and a serum half-life of 5 hours.

Serum half-life is relevant if a patient develops chest pain after a PDE5I is taken. Nitroglycerine must be withheld for at least 24 hours for Sildenafil and Vardenafil, 48 hours for Tadalafil, and 12 hours for Avanafil.

Tmax is relevant to the amount of time that a patient must wait between taking the medication and attempting sexual intercourse.

How are PDE5I metabolized? Why is this clinically relevant?

1. These agents are metabolized by the cytochrome CYP4A4 system
2. Dose reduction may be necessary in men taking CP450 inhibitors (Ketoconazole, Erythromycin, Ritonavir, Indinavir, grapefruit juice)
3. Other agents like Rifampin, Phenobarbital, Phenytoin, and Carbamazepine may enhance the metabolism of PDE5I
4. Men with severe hepatic or renal dysfunction (glomerular filtration rate <30mL/min) should start at the lowest dose

You prescribe Sildenafil 50mg to the patient and he takes it 3 times with no improvement. Next step?

1. Non-responders to PDE5I may be due to lack of efficacy but are often due to incorrect usage. Inquire where he is obtaining the medication, as many patients obtain ineffective black market agents for cost reasons
2. Ensure that the patient understands that PDE5I are not initiators of erection and require sexual stimulation to facilitate an erection
3. Make sure they wait an adequate amount of time between taking the medication and attempting sexual intercourse

4. Additionally, absorption of Sildenafil and Vardenafil can be delayed by a meal. Tadalafil absorption is unaffected by food. After ensuring appropriate usage, increase the dose

After taking Sildenafil 100mg properly multiple times, he has mild improvement in penile rigidity, but still no ability to penetrate. He has similar results with Tadalafil 20mg. He is frustrated that pills work for his friends but not for him. He would like to know why he has ED before proceeding with further therapy.

What specialized diagnostic tests are available?

Specialized diagnostic tests are not necessary to treat most patients with ED. However, they can be helpful in complex clinical presentations seen by specialists.

1. Duplex Doppler ultrasound of the penis
   a. This test is the most reliable and least invasive diagnostic modality for assessing ED
   b. It is performed with a 7–10 Hz transducer to image the penis starting 5–10 minutes after intracavernous injection of an erectogenic medication
   c. The goal is to administer enough medication to image the penis while it is at least as erect as the patient's best quality erection
   d. Both cavernosal arteries should be imaged with the probe-vessel angle at 60°
      i. A normal cavernous artery peak systolic velocity (PSV) of >35cm/s rules out arterial insufficiency as the cause of ED
      ii. A normal cavernous artery end diastolic velocity (EDV) of <5cm/s rules out venous insufficiency as the cause of ED
   e. Variations on the technique involve assessing PSV and EDV at baseline and every 5 minutes after injection up to 20 minutes, assessing cavernous artery diameter (normal >0.7mm) to evaluate for arterial insufficiency, and using a resistive index [(PSV-EDV)/PDV)] <0.75 to evaluate for venous insufficiency
   f. The authors think a well performed ultrasound focusing on the PSV and EDV provides the functional information necessary
2. Combined intracavernosal injection and stimulation
   a. Patient undergoes intracavernosal injection of an erectogenic medication and stimulates himself
   b. A positive result is an erection hard enough for penetration that lasts for 30 minutes
   c. A positive test rules out venous insufficiency but does not rule out arterial insufficiency
   d. A negative test can be due to arterial insufficiency, venous insufficiency, anxiety, and inadequate dosing
   e. Because the test is often inconclusive as a diagnostic test, duplex Doppler ultrasound is preferred
3. Dynamic infusion cavernosometry and cavernosography (DICC)
   a. This test is the most sensitive test for venous insufficiency; however, it is only performed in men who are being considered for vascular reconstructive surgery
   b. It involves placing 2 needles into the corpora following injection of an erectogenic medication and measuring the flow of heparinized saline required to maintain an erection of at least 150 mm Hg
   c. The flow required is normally <3ml/min in the absence of venous leak
   d. Once the pressure of 150 mg Hg is obtained, the flow of saline is ceased, and the fall in intracorporal pressure over the next 30 seconds is measured. The pressure decay should be <45 mm Hg in the absence of venous leak

   e. Alternatively, the inability to increase the intracavernosal pressure to the mean arterial pressure indicates venous leak. Cavernosography is then performed to identify the site of venous leak by infusing radiographic contrast to maintain flow and obtaining AP and oblique images

4. Pudendal arteriography
   a. This test is used in young men who have suspected arterial insufficiency due to a site-specific lesion that can be bypassed
   b. After injection of an erectogenic agent to maximally dilate the penile arterial supply, the bilateral pudendal arteries are cannulated and injected with radiographic contrast to evaluate for penile arterial stenosis. The inferior epigastric vessels are also evaluated for patency for use in surgical revascularization
5. Nocturnal penile tumescence and rigidity monitoring
   a. This test can help distinguish psychogenic from organic ED and is performed over 2 nights
      i. Conventionally, the test is done in a sleep lab after applying nocturnal monitoring devices that measure the number and duration of erections, as well as tumescence and maximal rigidity
   b. Rigiscan is an automated portable device for use at home
      i. Criteria for a normal test include at least 4 erections longer than 30 minutes per night, with a circumference increase at least 3 cm at the base, 2 cm at the tip, and maximal rigidity >70%
      ii. This test does not correlate well with sexual performance and is not routinely used
6. Penile biothesiometry
   a. This test assesses the afferent sensory function of the penis. It is useful when patients have ED associated with sensory complaints such as numbness
   b. The device provides a gradually increasing amount of vibratory stimulation to the pulp of the index fingers (as a control), both sides of the penile shaft, and the glans penis
   c. Device specific thresholds of normal are used to assess normal function of the afferent sensory nerves (dorsal penile nerve via the pudendal nerve)

The patient undergoes a penile duplex Doppler ultrasound. He receives 5 units of Trimix resulting in an erection hard enough for penetration. His PSV is 20 cm/s and his EDV is -5cm/s.

What is your assessment and recommendation?

The patient has arterial insufficiency, likely non-focal since he has multiple cardiovascular comorbidities and no history of trauma.

He failed a trial of PDE5I therapy and should be re-informed about the benefits and risk of other therapies, including vacuum erection devices, intraurethral Alprostadil suppositories, intracavernous drug injection, and penile prosthesis.

These should be applied in a stepwise fashion with increasing invasiveness and risk balanced against the likelihood of efficacy.

The patient elects a trial of intraurethral Alprostadil.

How would you counsel him on efficacy, side effects, contraindications, and instructions?

Intraurethral Alprostadil achieves erections hard enough for penetration in 50% of men, but its use is limited by the side effect of penile pain in 33% of men. Hypotension can occur in 3% of men, so the first dose must be administered under the supervision of a health care provider. Other side effects include urethral bleeding (5%), priapism (<1%), and UTI (<1%).

Contraindications include structural abnormalities such as urethral stricture, penile angulation or fibrosis, infections (balanitis or urethritis). A condom must be used during sexual activity with a pregnant woman.

After administering the first dose in the office without adverse effects, you titrate him from 125 mcg to 1000 mcg with some improvement; however, he is still unable to achieve erections hard enough for penetration. He expresses interest in a vacuum erection device.

How would you counsel him?

Efficacy rates are 67–90%, but satisfaction rates are 34–68%. The patient should be advised to obtain a device that has a vacuum limiter, which prevents penile injury by preventing excess negative pressure. He should limit its use to 20–30 minutes.

Confirm the patient does not have a bleeding disorder and is not on an anticoagulant. Side effects include pain, inability to ejaculate, petechiae, bruising, and numbness.

After using the vacuum erection device as directed, he is not happy with the result and expresses interest in intracavernous injection (ICI) therapy.

What preparations are available?

1. Alprostadil
   a. Only FDA approved drug for ICI and is the only drug used in monotherapy for ICI
   b. It works by activating adenylate cyclase and increasing intracellular cyclic AMP
   c. As monotherapy, its efficacy is 70%
   d. Side effects include pain (37%), priapism (5%), and fibrosis (3%). Injection site ecchymosis (2%) and hematoma (3%) are risks of all ICI preparations
2. Phentolamine
   a. An α-adrenergic receptor inhibitor not effective as monotherapy
   b. Inhibits detumescence, thus potentiating the effects of other medications
   c. Used in combination with Papaverine, commonly referred to as Bimix
3. Papaverine
   a. A non-specific PDE inhibitor not used in monotherapy
   b. Unlike Alprostadil, it does not cause penile pain, but it is metabolized by the liver and can rarely result in liver enzyme elevation
   c. Abandoned as monotherapy because of its limited effectiveness. Bimix usually refers to Papaverine and Phentolamine, which has an efficacy of 90% and no penile pain
4. Trimix
   a. A formulation of Alprostadil, Phentolamine, and Papaverine
   b. Efficacy is 92% with similar side effects to Alprostadil monotherapy except for less penile pain

What are the advantages and disadvantages of ICI monotherapy versus combination therapy?

Monotherapy with Alprostadil is readily available at many pharmacies, whereas combination therapies are only available at pharmacies with compounding services.

Combination therapy increases efficacy while decreasing side effects. Final choice is based on efficacy, side effects, and cost.

The patient is interested in combination therapy with Trimix.

What are contraindications to ICI? How will you instruct the patient on the use of ICI?

Ensure that the patient is not using Monoamine Oxidase Inhibitors (MAOIs), such as Phenelzine, since α-adrenergic agonists used to treat prolonged erection/priapism can lead to life threatening hypertensive crisis if administered to men using MAOIs.

Relative contraindications to ICI include poor manual dexterity or visual acuity. Men on Aspirin and Warfarin should use caution to prevent hematoma and ecchymosis.

The initial dose of ICI should be administered under the supervision of a healthcare provider. Briefly, wipe the site of the injection with alcohol, inject the medication at the dorsal 10 o'clock or 2 o'clock locations to avoid the penile vessels, neurovascular bundles, and the urethra, and hold pressure for 2–3 minutes (5–6 minutes for men on blood thinners).

Have the patient self-stimulate and assess response after 15 minutes. Use response to titrate dose over subsequent injections. Do not let the patient leave the office until he has detumesced. Part of the counseling process with ICI must include instruction for identification of priapism and a plan of action in the event of prolonged erection.

Using Trimix the patient achieves an erection hard enough for penetration that lasts 30 minutes; however, he complains of a bothersome penile burning sensation when he uses the medication.

Next step?

Switching the medication from Trimix to Bimix will greatly reduce the chance of penile pain with ICI use due to the removal of the offending agent, Alprostadil.

Despite its efficacy, the patient is unhappy with using ICI and is interested in a penile prosthesis.

How would you counsel him about its effectiveness?

Penile prosthesis insertion is associated with high efficacy and high satisfaction (92–100%). However, the patient needs to know that there will be differences from the normal flaccid and erect penis (i.e., the glans penis does not increase in size). Furthermore, the penile prosthesis insertion is irreversible, i.e., if ever removed will result in failure of any future pharmacotherapy.

What are the types of penile prosthesis and how do they differ?

The 2 classes of penile prosthesis are inflatable (2 and 3-piece) and malleable devices (semi-rigid).

3-piece inflatable devices include a reservoir usually placed in the retropubic space. 3-piece devices are considered more physiologic in that the cavernosal cylinders completely empty when not in use and completely fill when activated.

However, there is a risk of injuring adjacent structures when placing the retropubic reservoir, especially in a fibrotic space post-surgery or radiation. This risk is decreased by placing the reservoir in the ectopic position anterior to the transversalis fascia, which does carry the possibility of a bulge being visible at the site of the reservoir.

2-piece inflatable devices consist of the cylinders and the pump without a reservoir. They provide less rigidity and less flaccidity than a 3-piece, but do not carry the risk associated with placing a reservoir.

Malleable prosthesis are flexible cylinders placed in each corpora that allow for manipulation into the flaccid or erect positions. They are the least physiologic; however, they are associated with less complications like infection or mechanical failure.

What are the surgical approaches used to insert a penile prosthesis?

1. Penoscrotal approach
   a. Allows for corporotomies that are more proximal, making the cylinder tubing less palpable
   b. It is also on the ventrum of the corporal bodies, hence there is low risk of injuring the dorsal nerves and causing penile numbness
   c. This approach also allows direct visualization of the pump placement
   d. The disadvantage of this approach is that the reservoir is often placed in a blind fashion because of the distance from the inguinal canal, which is perforated to place the reservoir in retropubic fashion
2. Infrapubic approach
   a. Has the advantage of allowing direct visualization of the reservoir placement
   b. However, the pump may be more challenging to place, the dorsal nerves are more at risk of being injured, and the cylinder tubing may be more likely to be palpable if the corpora are not opened proximally
3. Subcoronal incision can be used for malleable prosthesis placement
   a. A subcoronal circumcising incision for placement of inflatable prosthesis has been described but is not widely used

What are reasons to delay the placement of a penile prosthesis?

Delay the procedure in the presence of systemic, cutaneous, or urinary infection. Consider delaying if diabetes can be better controlled.

What are intraoperative steps used to minimize the chance of infection?

1. Administer gram-negative and gram-positive coverage preoperatively
   a. The preferred antibiotic regimen is an Aminoglycoside + (1st/2nd generation Cephalosporin or Vancomycin)
2. Shave the operative area immediately prior to surgery
3. A 10-minute skin prep is often performed followed by use of alcohol based final skin prep

Describe the potential intraoperative complications of penile prosthesis placement and their management.

1. Urethral perforation
   a. Usually detected with blood at the meatus or hematuria
   b. Stop the procedure and leave a urethral catheter for 7–10 days
2. Corporal crossover
   a. Occurs when dilating the corpora if the septum is inadvertently perforated

   b. You do not have to abandon the procedure. Leave a dilator in the side which is crossed over into re-dilate the side from which the cross over emanated, focusing on the dorsolateral surface of the corpus cavernosum
3. Crus perforation
   a. Happens during proximal dilation when the dilator travels into the perineal soft tissue. Options for correction include:
      i. Create a mesh wind sock to buttress the rear tip of the cylinder and secure this to the tunica albuginea
      ii. Secure the rear of the implant itself or a rear tip extender to the tunica albuginea with a suture tied long enough hold cylinder in the correct location
      iii. Close the corpora snugly around the tubing (only with small perforations)

What postoperative complications are associated with penile prosthesis insertion? How are they managed?

1. Infection occurs in 1–3% of procedures
   a. Early infection present within weeks postoperatively with fever, pain, swelling, or purulence. These will usually grow gram-positive bacteria
   b. Late infection presents months after the infection with chronic pain or skin fixation over the tubing or pump. An elevated WBC or erythrocyte sedimentation rate (ESR) may be present with either early or late infection
   c. Infected prostheses are managed by removal of the entire device
2. Malfunction occurs in 15–20% of devices at 10 years
   a. Managed with replacement of the device or part of the device if the pump alone is defective
3. Erosion is more common in men who lack penile sensation (paraplegia, diabetes) and is more common with malleable devices
   a. Managed by removing the eroded cylinder and replacing it
   b. Many men are able to function with a unilateral cylinder and elect not to undergo a subsequent procedure
4. Poor glans (support) is also known as SST deformity (supersonic transporter) and is the result of insufficient distal dilation or under-sizing of the cylinders
   a. The definitive management is removing the cylinders, re-dilating, and correctly sizing
   b. Minor cases can be corrected with glans plication to the penile shaft
5. Buckling or S shaped deformities result from oversizing of the cylinders
   a. Oversized cylinders can also cause chronic pain
   b. Corrected by replacing the cylinders with an appropriate size device.
6. Auto-inflation occurs when physical activity partially inflates the device
   a. This complication can be managed by replacing the device with a newer device
   b. Newer devices have lockout mechanisms in either the pump (AMS) or the reservoir (Coloplast)

Your patient presents 3 months after placement of a 3-piece inflatable penile prosthesis with chronic pain ever since the operation that is exacerbated by inflation. The patient had no other complaints and has a normal exam except for a tender phallus. His GU exam is negative for erythema, edema, fluctuance, and pump fixation to the scrotal skin.

What tests would you order?

Urinalysis, urine culture, serum chemistries, and CBC. An ESR can also be helpful.

All tests are normal with the exception of WBC of 12 (70% neutrophils) and an ESR of 80 mm/hr (normal 0–20).

What is your assessment and plan?

He likely has a late infected penile prosthesis. He should be admitted and placed on broad spectrum IV antibiotics. All components of the device of the device should be cultured and removed.

His options include removal of the prosthesis alone, removal and immediate salvage, and removal with re-implant at a later date. Afterwards, he should be treated with culture specific antibiotics.

What is immediate salvage and how successful is it?

Immediate salvage means removing the infected prosthesis, copiously irrigating the wound with multiple antibiotic solutions, and inserting a new prosthesis at the same setting. Successful in about 80% of cases.

What are problems with delayed re-implantation and how can they be minimized?

This results in secondary corporal fibrosis, decreased penile size, and a more challenging procedure during the reinsertion. This can be minimized by performing the second procedure as soon as the postoperative edema and healing have occurred (6–12 weeks postop).

CASE 2

HPI: A 66-year-old man presents to the emergency room with a painful erection that has lasted 8 hours. He is 10 months status post a retropubic radical prostatectomy and has been using Trimix ICI therapy for the past 6 months to assist with recovery of erectile function. When he started therapy 6 months ago, he was titrated to a dose that enabled erections hard enough for penetration and lasted about 30 minutes. He noticed that for the past month he has had erections almost hard enough for penetration even without the use of Trimix. He has not seen his urologist for 3 months and was not aware that the dose may need to be adjusted as his nerves recover.

PMH: prostate cancer; coronary artery disease; transient ischemic attack; hypertension

PSH: retropubic radical prostatectomy with bilateral nerve sparing; coronary artery bypass surgery 7 years ago; left open inguinal hernia repair

FH: father with diabetes
SH: (-) tob; (-) ETOH; retired taxi driver
ROS: (-)

Allergies: none **Medications:** Coumadin 2.5 mg daily, sublingual Nitroglycerin as needed, Metoprolol succinate 25mg daily

PE:

Vitals	T 99.7	P 90	BP 130/70
GA	awake, alert, in distress; normal masculine hair distribution		
Abdomen	soft; non-tender; non-distended		
GU	firm, rigid, tender circumcised phallus; normal meatus; normal firm 16 cc testes bilaterally		

What is your assessment?

This patient has priapism, likely ischemic priapism given his history of Trimix use. His dose of Trimix was titrated while his erectile function was poor post-prostatectomy. Now that he is recovering function, his dose should have been titrated down.

Define priapism and the different subtypes.

Priapism is an erection that lasts longer than 4 hours and is unrelated to sexual stimulation. Subtypes include ischemic, non-ischemic, and stuttering priapism.

Ischemic priapism is a non-sexual, persistent erection with little or no cavernous blood flow. The condition is painful, and on exam the corpora are rigid and tender to palpation. This is an emergency, and resolution is characterized by a flaccid, non-painful state; however, edema, ecchymosis, and partial erection may persist. Resolution can be confirmed by arterial blood gas (ABG) or color duplex ultrasound.

Non-ischemic priapism is a non-sexual, persistent erection caused by unregulated cavernous arterial inflow. The condition is not painful, and on exam the corpora are not fully rigid or tender. Antecedent trauma is common. This is not an emergency and resolution is demonstrated by return to a completely flaccid state.

Stuttering priapism is a recurrent form of ischemic priapism often associated with sickle cell disease and is an indication to explore preventative measures.

What are risk factors to ask about in the history?

1. Ask about hematologic disorders such as sickle cell disease, thalassemia, or leukemia
2. History of trauma to the pelvis, genitalia, or perineum is noteworthy
3. Use of drugs such as ICI of vasoactive erectile agents, anti-hypertensives, anticoagulants (Warfarin, Heparin), antidepressants and anxiolytics (Trazodone, anti-psychotics), α blockers, recreational drugs (cocaine) have all been reported to be associated with priapism

What is the next step in evaluation?

The most important step is determining whether the priapism is ischemic or non-ischemic, as the treatment options are very different. This can be done either with cavernosal blood gas sampling or color duplex ultrasonography.

Cavernosal blood gas values indicative of ischemic priapism are a P_{O2} <30 mm Hg, a P_{CO2} >60 mm Hg, and a pH <7.25.

Color duplex ultrasonography can also be used to differentiate ischemic from non-ischemic priapism. The ultrasound will show lack of significant blood flow in the cavernosal arteries, whereas non-ischemic priapism patients have normal or high blood flow in these arteries and the presence of a cavernous artery-cavernosal space fistula.

What laboratory tests would you order?

1. A CBC should be ordered to assess hematologic causes
2. Unless another clear cause of priapism is identified from history, order a reticulocyte count since it will be elevated in men with sickle cell disease
3. Also order hemoglobin electrophoresis, which will identify hemoglobinopathies like thalassemia
4. Consider a urine drug (for cocaine presence) and psychoactive medication screen

The patient's serum laboratory tests are normal, and his cavernosal blood gas reveals a P_{O2} of 25 mm Hg, a P_{CO2} of 83 mm Hg, and a pH of 7.17.

How do you proceed?

This patient has ischemic priapism and should be counseled about the potential risk of ED from the condition itself. The treatment should progress in a stepwise manner from least invasive to most invasive; however, systemic oral therapy is not indicated for the treatment of ischemic priapism.

In general, the first step should either be corporal aspiration (with or without irrigation) or intracavernosal injection of a phenylephrine. However, this patient has a history of coronary artery disease and transient ischemic attacks. Start with aspiration and irrigation using a 19 gauge needle placed through the glans into the corpus cavernosum or laterally avoiding the penile neurovascular bundles.

His priapism persists despite corporal aspiration and irrigation.

Next step?

Intracavernous injection of Phenylephrine.

Prior to doing this, you need to have blood pressure and electrocardiogram monitoring since he has high cardiovascular risk.

Furthermore, you need to confirm the patient is not on a MAOI. Sympathomimetic use in patients with MAOIs can result in hypertensive crisis and subarachnoid hemorrhage. The dose of Phenylephrine is 100 to 500 mcg/mL; however, given his cardiovascular risk, start at the lowest dose and inject slowly. Inject 1 mL every 3–5 minutes for about 1 hour.

Why choose phenylephrine? What are its side effects?

Phenylephrine is a pure α-1 agonist, and thus lacks β-mediated cardiac effects seen with Epinephrine. Due to its safety profile, it is the sympathomimetic of choice. It can cause hypertension and reflex bradycardia.

The priapism persists despite multiple injections of Phenylephrine.

Next steps?

The next step is a distal caverno-glanular shunt (unilaterally first, then bilateral if not successful).

Percutaneous distal shunts include the Winter (large biopsy needle), Ebbehoj (multiple punctures with an 11 blade scalpel), T-shunt (insert 10 blade scalpel vertically and rotate 90° lateral away from urethra), and T-shunt with corporal tunneling (also known as a "snake maneuver") using up to a 20F sound.

Open distal shunts include the Al-Ghorab (glans incision and excision of the tip of the cavernosum) with or without tunneling.

Penile edema can persist after these interventions, making it difficult to determine whether the shunt procedure was successful. Color Doppler ultrasound or cavernosal blood gas can be helpful in confirming resolution of priapism.

If a distal shunt is unsuccessful at correcting the priapism, a proximal shunt can be performed. Either a Quackles (cavernospongiosum shunt) or a Grayhack (cavernosaphenous shunt) can be performed.

When is immediate penile implant surgery indicated?

The chance of post-priapism ED increases with duration of ischemia.

Some experts recommend considering immediate penile implant surgery when ED is inevitable. The penile scarring and shortening that can result from priapism can make later penile implant placement difficult.

The 2003 AUA Guidelines on Priapism do not address the topic. The AUA Core Curriculum states that immediate penile implant surgery can be considered after 24 hours of ischemia. The EAU Guidelines say to consider it after 48 hours. Both documents recommend an MRI prior to surgery or a corporal biopsy at the time of surgery to document corporal smooth muscle necrosis.

How does your management of ischemic priapism change if an underlying disorder like sickle cell disease is present?

Your management of ischemic priapism does not change. You can manage other conditions concurrently but do not delay your penile intervention.

For a patient with sickle cell disease, you can support with concomitant hydration, oxygen, and alkalinization, but not if it delays corporal aspiration or injection of phenylephrine.

How does your management of recurrent ischemic priapism change in the acute setting? What would you recommend for prevention of stuttering priapism?

Again, your management does not change in the acute setting. After the acute priapism is managed as above, androgen ablation therapy with an LHRH agonist, GnRH antagonist, anti-androgen, or Ketoconazole (with Corticosteroid supplementation) can reduce future priapism episodes.

This strategy is contraindicated for men trying to conceive and boys who have not completed their growth and sexual maturity. These patients should also be taught at-home, self-administration of intracavernous Phenylephrine.

How is the management of non-ischemic priapism different than ischemic priapism?

Non-ischemic priapism is not an emergency and should be observed as it often resolves. Initially, you should recommend conservative management with ice-packs and site-specific compression to the fistula site.

If the condition does not resolve and the patient requests intervention, the next step is selective arterial embolization with a non-permanent substance (autologous clot). Should this fail, embolization with permanent coils is indicated. Surgical management, a last resort, involves fistula localization with ultrasound and selective ligation.

CASE 3

HPI: 57-year-old heterosexual man presents with penile curvature. He first noticed pain with erections 3 months ago, but did not think much of it. A month ago, his wife, a 57-year-old woman, started complaining about vaginal discomfort during penetrative sexual activity. They noticed that his penis curves to the right about 90°. While he has always had a slight rightwards curvature, this is a change from 3 months ago, and they do not remember any traumatic events. He has not noticed any instability during attempts at penetration. His erections are not as rigid as they used to be. He is not rigid enough without a PDE5 inhibitor, but his hardness is sufficient for penetration with sildenafil, which he started 2 years ago. His orgasm and ejaculation are normal.

PMH: hypertension; hyperlipidemia; denies Dupuytren's contracture

PSH: none

FH: father died of colon cancer in his 70s
SH: (-) tob; (+) ETOH, 2 drinks a day; no illegal substance use; real estate agent
ROS: no other pertinent symptoms

Allergies: none **Medications:** Lisinopril, Simvastatin, Sildenafil PRN
PE:

Vitals	P 71 BP 119/78
GA	awake and alert; normal masculine hair distribution
Chest	no gynecomastia
Heart	RRR; no murmurs
Lungs	clear
Abdomen	soft; non-tender; non-distended
GU	circumcised phallus; 1 cm plaque on the right corpora in the mid ⅓ of the penile shaft that is tender to palpation; stretched flaccid penile length (pubic bone to coronal sulcus) is 13 cm; normal meatus, normal firm 15 cc testes bilaterally; normal 30 cc prostate
Extremities	no signs of Dupuytren's contracture on hands or Lederhosen's disease on plantar fascia; intact femoral and pedal pulses

Any other historical information needed?

It is important to note the degree of distress experienced by the patient. This can take the form of psychological distress (embarrassment about physical appearance, self-image, and confidence) and physical impairment (inability to have sexual intercourse, constraint in positions possible, impairment of sexual function due to pain for either patient or partner). This will direct treatment decisions.

This couple reports they used to be sexually active every other week, although this past month they stopped because of pain with erection and vaginal discomfort.

What are your options for evaluating the degree of baseline curvature?

An accurate assessment of the deformity is necessary to characterize the type of deformity (uniplanar or biplanar, hourglass deformity), the severity, and the stability (buckling with penetration). Options to evaluate the degree of curvature are patient report, photographs taken at home, applying a vacuum erectile device in the office, or intracavernous injection.

Penile deformity is most accurately assessed with the penis at maximum erectile rigidity. Thus, intracavernous injection is the most accurate method and is strongly recommended before any invasive intervention. Duplex Doppler ultrasound is optional at the time of injection, but is helpful in defining erectile function as well as presence of calcifications.

The patient is administered 5 units of Trimix and achieves an erection that is 90% rigid, which is his maximal rigidity when using Sildenafil. His deformity is a right sided 45° curvature in the middle ⅓ of his penile shaft. There is no instability or hourglass deformity. Ultrasound reveals a peak systolic velocity of 40cm/s bilaterally, and end diastolic velocity of -5 cm/s bilaterally. No calcifications are present.

How would you counsel him on the natural history of his conditions and the range of treatment options?

The patient is in the active phase of Peyronie's disease. The natural history of the disease is that 50% will have stable deformity, 40% will worsen, and 10% will improve.

In general, the treatment options for Peyronie's disease are observation, intralesional injection of Verapamil or interferon α-2b, intralesional injection of collagenase clostridium histolyticum, tunical plication, plaque incision/excision with or without grafting, and penile prosthesis surgery.

The only treatment options appropriate for patients in the active phase are observation and intralesional injection of Verapamil. The 2015 AUA guidelines do not recommend oral therapy, and do not make recommendations about mechanical therapies like traction devices.

What are his treatment options for his pain?

You should offer him non-steroidal anti-inflammatory medications for the management of pain in the active phase. You may also offer penile shock wave therapy to improve penile pain, although this is rarely used in the U.S. since it has no effect on the deformity and has adverse events such as localized bruising or urethral bleeding.

The patient is eager to proceed with an intervention at this time.

What are his options and their risks and benefits?

For patients who elect treatment in the active phase, you can recommend intralesional injections of Verapamil. Verapamil is a calcium channel blocker, and its therapeutic benefit in Peyronie's disease is thought to be by modulating the transport of extracellular matrix molecules and inhibiting fibroblast formation.

Intralesional Verapamil results in a reduction in curvature in 20% of patients and a stabilization of curvature in 60% of patients. Adverse events include penile pain at the injection site in 15% of patients, bruising in 25% of men, and dizziness/nausea in 10% of men.

The patient would prefer to try an oral therapy for Peyronie's prior to any intralesional therapies.

What are appropriate therapies to offer?

You should not offer oral therapy to patients, including vitamin E, vitamin E with L-carnitine, Procarbazine, Tamoxifen, or omega-3 fatty acids. These therapies have not been shown to improve pain, curvature, or plaque in Peyronie's disease.

The patient elects treatment with intralesional Verapamil. He undergoes 12 treatments of 10 mg in 5 mL sterile saline every 2 weeks. His pain resolves and his curvature remains unchanged at 45° at a curvature assessment.

He is now a year from the onset of his symptoms and has had stable curvature for 6 months.

He would like to know what non-surgical options are available.

The patient has stable disease now and is a candidate for intralesional injection of interferon α-2b, intralesional injection of collagenase clostridium histolyticum, tunical plication, plaque incision/excision with or without grafting, and penile prosthesis surgery.

Except for penile prosthesis surgery, all these treatments are for men with intact erectile function (with or without medication).

1. Intralesional interferon α-2b is a cytokine thought to inhibit the proliferation of fibroblasts
   a. Effective at improving curvature, pain, and plaque size; reduces curvature by 13.5°
   b. Similar to collagenase clostridium histolyticum, it is recommended in men with stable disease and curvature >30° without a calcified plaque

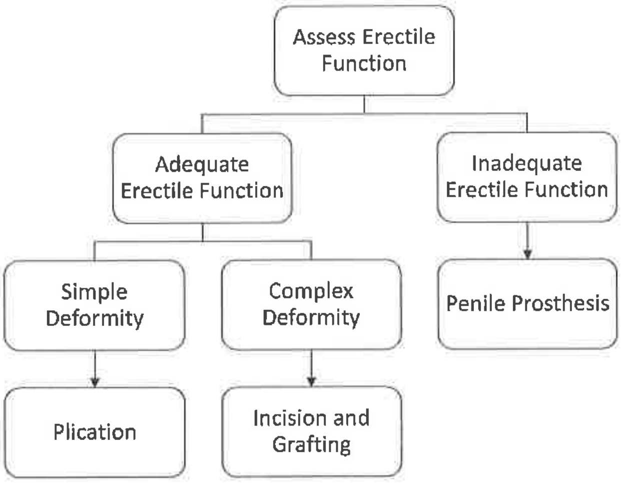
   Note: Warn patients that 40% to 100% of men will have flu-like symptoms and minor penile swelling.
2. Intralesional collagenase clostridium histolyticum in combination with modeling is the first FDA approved treatment for Peyronie's disease
   a. Approved for men with stable disease and curvature >30° and <90°
   b. Average improvement in curvature is 35%, with 75% of men obtaining ≥25% improvement
   c. It has not been studied in men with hourglass deformity, calcified plaques, ventral plaques or acute phase disease
   d. Adverse events are experienced by 85% of patients and include bruising (80%), penile swelling (50%), and penile pain (50%). Additionally, 0.5% of men experienced corporal rupture, hence the recommendation for 2 weeks without sexual activity after each treatment

The patient elects intralesional injection of collagenase clostridium histolyticum and completes 4 treatment cycles. He tolerates the treatment well. On repeat curvature assessment, his curvature is 40° and he still experiences significant psychological and functional bother.

He would like to discuss surgical treatment options.

Surgical treatment of Peyronie's disease is indicated in patients with stable phase deformities that impair sexual function, deformities not amenable to medical therapy (calcified plaques, instability), and patients who have failed medical therapy. The decision of what type of surgery to perform depends on the patient's erectile function.

Figure. Simplified approach to the surgical management of Peyronie's Disease



1. Penile prosthesis

   If the patient does not have erections adequate for sexual activity, he should be counseled to undergo an inflatable penile prosthesis insertion. If the insertion of the prosthesis alone does not address the deformity sufficiently, you should be able to perform adjuvant maneuvers like molding, plication, and incision/grafting.

   In general, these adjuvant maneuvers are required when the deformity is still >30° after insertion of the prosthesis. Satisfaction rates after penile prosthesis surgery are 80%, slightly less than those inserted for ED alone. The adverse event rates are similarly low compared with non-Peyronie's cases.

2. Men with adequate erectile function can undergo either plication or incision and grafting depending on the complexity of their deformity.

   Plication involves shortening the convex side of the penis to match the shorter side. A variety of techniques have been described, including (among others): (1) the Nesbit (excising an ellipse); (2) a vertical incision that is closed horizontally (Yachia); and (3) a dot technique that imbricates the tunica. The reported success rates are over 90%.

   While the final penile length should match the stretched flaccid penile length preoperatively, many patients perceive loss of penile length because the shortening that has occurred due to their disease.

   Adverse events are low, with palpable permanent sutures (10%) being the most common complaint. As with any penile surgery, be aware that the urethra ventrally and neurovascular bundles dorsolaterally must be avoided.

   Complex cases that are appropriate for plaque incision and grafting are destabilizing hourglass or hinge effects, large plaques, curvature >60°, and short penile length.

   Plaque incision and grafting involves incising or excising the plaque at its point of maximal curvature and repairing the defect in the tunica albuginea with a non-synthetic graft like processed pericardium or small intestinal submucosa. The majority of studies report improvement rates of over 80%, with patient satisfaction at over 80% as well.

The procedure can impair erectile function, which is why it is reserved for patients with intact erectile function. Adverse events are ED in up to 50% of men, hematoma in <10% of cases, and diminished sensation in <5%.

What surgical technique would you recommend to this patient?

He has intact erectile function with Sildenafil. He has a stretched penile length of 13cm, and a right curvature of 40°. He has a simple plaque. The patient undergoes a penile plication with a dot technique that results in curvature <10° and the patient is satisfied with his result.

CASE 4

HPI: 21-year-old heterosexual man presents with orgasmic dysfunction. He is monogamous with a 21-year-old female partner whom he has been dating for 3 months. She is not present at the office visit. They are sexually active 4 days a week. He is presenting because they recently had penetrative vaginal intercourse, and he feels he has an orgasm too quickly. He has good libido.

PMH: none
PSH: none

Allergies: none **Medications:** none

SH: (-) tob; (+) ETOH, 5 drinks a day during weekends; occasional marijuana use; undergraduate student
FH: none
ROS: no symptoms of thyroid dysfunction

PE:

Vitals	P 80	BP 90/50
GA	awake and alert; normal masculine hair distribution	
Chest	no gynecomastia	
Heart	RRR, no murmurs	
Lungs	clear	
Abdomen	soft; non-tender; non-distended	
GU	normal circumcised phallus; normal meatus; normal firm 18 cc testes bilaterally, no varicocele bilaterally	
Extremities	intact femoral and pedal pulses	

What further aspects of his medical history are important?

1. You need to determine the length of time between penetration and ejaculation, known as the intravaginal ejaculatory latency time (IELT). It is helpful to have the partner corroborate the IELT
2. Premature ejaculation (PE) is defined by the International Society of Sexual Medicine as: ejaculation that is almost always within 1 minute of vaginal penetration, causing person distress or relationship discord
   a. Ask about ability to control ejaculation. PE is characterized by an inability to delay ejaculation, meaning that the short IELT is not by choice (rushed environment, partner discomfort)
3. Another important aspect is to determine whether the patient has functioned with loss of sustaining capability rather than PE
   a. For example, inquire if the patient is in a rush to finish sexual activity because of inability to sustain an erection
   b. In men with both conditions concomitantly, ED should be treated first, as this may also improve the PE
   c. Furthermore, do not misdiagnosis PE as ED
4. The duration of PE differentiates lifelong PE from acquired PE
   a. Lifelong PE is associated with altered sensitivity of central nervous system serotonergic receptors. Lifelong PE is treatable, but unlikely to be curable

   b. Acquired PE is more associated with either a medical condition or a life stressor, and thus is more likely to be curable

The patient's IELT is 45 seconds. He has had a similar problem since he became sexually active 4 years ago. He does not have any difficulty with obtaining an erection.

What is your assessment and what laboratory workup can help confirm this?

The patient has lifelong PE and no associated ED. PE is a diagnosis made from history. You do not need to order any laboratory tests unless there is something about the history or physical exam that suggests hyperthyroidism, an uncommon condition in men that is associated with PE (although usually acquired PE).

What are the types of therapy that you can offer the patient? What are disadvantages of each therapy?

1. Psychotherapy/behavioral therapy is the first class of therapy
   a. Psychotherapy can address the issues associated with the onset of acquired PE, as well as address the stress to relationships that any form of PE can impose on a couple
   b. However, its long-term efficacy in men with lifelong PE is not as high as other forms of therapy. Similarly, behavioral therapy with the pause and squeeze technique can help in the short term, but does not typically provide long-term improvement
2. Topical anesthetics are another type of therapy for PE
   a. Topical Lidocaine and/or Prilocaine can be applied to the inside of a condom, worn for 20–30 minutes, and then washed off prior to sexual activity
   b. However, the loss of penile sensitivity, potential for transfer to partner, and need for application prior to sexual activity limit the long-term efficacy of this treatment modality
3. Oral antidepressants are the last type of treatment with proven efficacy for PE with IELT improvements of up to 70%
   a. Daily dosing is generally required, with PRN dosing not being shown to be very effective
   b. Specific medications that are well studied are Clomipramine and older selective serotonin reuptake inhibitors Sertraline, Fluoxetine, and Paroxetine
      i. Paroxetine is well tolerated and has the largest fold increase in IELT
      ii. None of these medications are FDA approved for PE
      iii. In Europe, Dapoxetine has regulatory approval for this indication, but it is not available in the U.S.
   c. Do not prescribe any of these medications to a patient using a MAOI since this could lead to serotonin syndrome
   d. Side effects of these medications include nausea, dry mouth, drowsiness, and reduced libido. Furthermore, you should counsel patients that these medications should be tapered rather than stopped to avoid withdrawal symptoms

You prescribe the patient Paroxetine 10 mg daily and he has a good response.

CASE 5

HPI: 63-year-old heterosexual man presents with 2 years of low libido and decreased energy. His primary care provider ordered a serum total testosterone, which was 250 ng/dL, and he was referred to you. He is sexually active with his wife, a 60-year-old woman, and he does not have difficulty obtaining erections hard enough for penetration. His orgasm and ejaculation are normal.

PMH: hypertension; hyperlipidemia; adult onset diabetes mellitus

PSH: cholecystectomy

Allergies: none **Medications:** Lisinopril, Metformin

FH: mother died from breast cancer in her 60s
SH: (-) tob; (+) ETOH, 1 drink a day; no illegal substance use; store manager
ROS: no symptoms of prolactinoma and thyroid dysfunction

PE:

Vitals: P 70 BP 133/61
GA: awake and alert; normal masculine hair distribution; BMI 31
Chest: no gynecomastia
Cardiac: RRR; no murmurs
Lungs: CTA
Abdomen: soft; non-tender; non-distended
GU: normal circumcised phallus; normal meatus; somewhat soft, 14 cc testes bilaterally; no varicocele bilaterally; normal 30 cc prostate
Ext: intact femoral and pedal pulses

Describe the mechanism by which testosterone is regulated in the body.

Gonadotropin-releasing hormone (GnRH), released from the hypothalamus, acts on the anterior pituitary gland to stimulate release of luteinizing hormone (LH) and follicle stimulating hormone (FSH), both of which act on the testes.

FSH acts on Sertoli cells to promote spermatogenesis. LH stimulates Leydig cells to produce testosterone.

Negative feedback to the hypothalamus and anterior pituitary is provided by both testosterone directly and its metabolite through aromatase, estradiol.

In what forms is testosterone found in the body? How does testosterone exert its action on the body?

60% of circulating testosterone is tightly bound to sex hormone binding globulin (SHBG) and is thus not bioavailable. Only 1–2% is free testosterone, whereas the remainder is loosely bound to albumin; both forms are considered bioavailable.

The androgen receptor binds both testosterone and its metabolite through 5-α reductase, dihydrotestosterone (DHT); although its affinity for DHT is greater. The complex of androgen and androgen receptor enter the nucleus to stimulate transcription.

What other aspects of his history would you like to know?

You are concerned about testosterone deficiency. Common symptoms are reduced sexual desire, tiredness (especially in the afternoon), mood alterations (irritability), decreased mental acuity, decreased strength and stamina and loss of muscle and increased fat deposition (central obesity). Unfortunately, none of these is specific to testosterone deficiency, which is why laboratory diagnosis is essential.

Confirm that the patient is not taking medications that can interfere with androgen production (opioids, corticosteroids). Inquire about surgeries to the testis or cranium. Ask about history of testicular insults like torsion, trauma, and orchitis or exposure to chemotherapy or testicular radiation.

Inquire what time the low testosterone lab value was drawn. Testosterone peaks in the early morning and has a subsequent decline during the day. While this diurnal variation is blunted in men over 40, it is still good practice to use morning testosterone values for diagnosis. Furthermore, testosterone deficiency can impair glucose metabolism, so also inquire about his HgA1c level and his glucose control.

Other symptoms he endorses upon inquiry are increased irritability and decreased mental acuity. He doesn't remember what time the testosterone labs were drawn, nor does he know his HgA1c, but he thinks his sugars are well controlled.

Next step?

You cannot diagnose testosterone deficiency with symptoms alone, you need biochemical confirmation. You can try to obtain the lab report from his primary care provider, who should also have his HgA1c level.

If the patient is seeing you without a history of laboratory evaluation, your initial test should be a total testosterone. It is worth noting that there are numerous assays for measurement of total and free testosterone levels.

The CDC recommends use of liquid chromatography tandem mass spectrometry (LC/MS-MS) for measurement of total testosterone and equilibrium dialysis for free testosterone measurement. Not all laboratories have such assays routinely available.

His primary care doctor faxes a report that says the blood was drawn at 9:30 AM and his total serum testosterone was 250 ng/dL and his HgA1c is 6.6.

Next step?

The threshold for what is considered a low serum testosterone concentration is controversial, but values above 350 ng/dL are generally considered normal. This patient's serum total testosterone was low, so the next step is to repeat the test with another morning total testosterone. In addition to the total testosterone, obtain an LH since this will help determine the type of testosterone deficiency.

Additionally, you can measure SHBG in older or obese men (who often have elevated SHBG), or men with borderline low testosterone. SHBG can be used to calculate the amount of free T. A free T <80 pg/mL is considered low.

You should also consider ordering a PSA in men over 40-years-old, and a TSH if the man's symptoms could also be consistent with hypothyroidism.

Prolactin should be ordered in men with severely low testosterone (<150 ng/dL), or men with new onset visual field defects.

Finally, order a baseline hematocrit in men who will likely be treated with testosterone replacement therapy.

The patient's repeat total testosterone is 215 ng/dL, his LH is 5 IU/L (normal), his SHBG is 30 nmol/L (normal), his hematocrit is 43% and his TSH is normal.

What are the classes of hypogonadism and which one does he have?

1. Hypergonadotropic hypogonadism (also known as primary hypogonadism) can be thought of a testicular failure. This condition is characterized by low testosterone despite elevated LH
   a. Examples include gonadotoxin exposure (chemotherapy, radiation therapy), congenital conditions (cryptorchidism, Klinefelter's syndrome), testicular insults (torsion, trauma, testicular cancer), and medications (Spironolactone, Ketoconazole)
2. Hypogonadotropic hypogonadism (or secondary hypogonadism) refers to testosterone deficiency associated with low LH levels, indicating that the problem is hypothalamic or pituitary in nature
   a. Classic examples include genetic disorders, (Kallmann's syndrome, Prader-Willi syndrome), trauma to the pituitary (pituitary tumor, prolactinoma, radiation, infarction), substances that cause negative feedback to the hypothalamus or pituitary (opioid use, corticosteroids, marijuana, anabolic steroids), and metabolic disorders (diabetes, obstructive sleep apnea, renal failure, malnutrition, obesity)
3. Finally, a mixed pattern of hypogonadism (compensated hypogonadism) refers to low testosterone in the presence of normal or borderline low LH. This is the most common hormone profile for men with adult onset hypogonadism

This man presents with adult-onset hypogonadism, also known as late-onset hypogonadism.

What are the physiologic effects of hypogonadism?

1. In addition to the symptoms described above, the patients can have decreased bone mass, sarcopenia, anemia, and impaired glucose metabolism
2. The relationship between adult onset hypogonadism and common comorbidities is complicated by the fact that the prevalence of hypogonadism and many comorbidities increases with age
3. High BMI, metabolic syndrome, and the number of a man's comorbidities are all associated with hypogonadism

This patient has symptoms consistent with hypogonadism and a biochemical profile consistent with hypogonadism.

What are the benefits to treatment of hypogonadism?

Men who are hypogonadal may experience the following benefits with treatment:

1. Sexual function (improvement in libido, erections, response to PDE5I)
2. Body composition (improved bone mineral density, decreased fat, increased skeletal muscle)

3. Psychologic (less depressive symptoms)
4. Cognitive factors (decrease in memory loss, greater attention span)
5. Comorbidity management (improve glucose control, lipid profile)

What are the potential risks associated with testosterone treatment?

It is clear that testosterone replacement therapy can negatively impact spermatogenesis, increase hematocrit, and cause gynecomastia (usually through elevated estradiol levels). The literature is less definitive regarding cardiovascular risk, increased prostate volume, and worsening obstructive sleep apnea.

1. Spermatogenesis
   a. Exogenous testosterone negatively impacts spermatogenesis by negative feedback causing decreased testicular production of testosterone
   b. While exogenous testosterone increases the serum testosterone, intratesticular testosterone is usually much higher than serum
   c. Exogenous testosterone decreases the intratesticular testosterone required for normal spermatogenesis and can also lead to testicular atrophy
   d. You must evaluate whether a man has completed his family prior to prescribing exogenous testosterone
2. Erythrocytosis
   a. Another common adverse event (2–7%) occurring with testosterone replacement
   b. Increase in hematocrit is proportional to the increase in serum testosterone
   c. Rates are higher with intramuscular testosterone injections than with transdermal agents
   d. Guidelines suggest maintaining serum hematocrit below 54%
3. Gynecomastia
   a. Can rarely occur through aromatization of testosterone into estradiol in <2% of men
4. Prostate volume
   a. May increase with testosterone; however, the majority of studies have not demonstrated any changes in flow rates or urinary symptom scores
5. Obstructive sleep apnea
   a. May worsen with testosterone replacement
   b. While there is no requirement for a sleep study prior to prescribing testosterone replacement, inquire about a history of the condition. The partner is often a more reliable historian in this regard
6. Cardiovascular risk
   a. Whether or not testosterone replacement therapy is associated with increased risk of cardiovascular events is an especially controversial topic
   b. There are no adequately powered trials with cardiovascular events as an endpoint
   c. The FDA felt that the signal suggested by 3 recent studies was sufficient to warrant a change to the labeling of testosterone products. Thus, it is advised to discuss the possibility of this with patients

What are the absolute contraindications for testosterone replacement therapy?

Guidelines recommend against treatment in men with prostate cancer, breast cancer, severe sleep apnea, hematocrit >50%, severe lower urinary tract symptoms, PSA>4 ng/mL, and male infertility, although none of these technically are an absolute contraindication.

The patient understands the risks and benefits of testosterone deficiency treatment and has no contraindications. While he is finished having children, he is concerned about the testicular atrophy that can occur with exogenous testosterone.

What other treatment options are there?

While not FDA approved for treatment of hypogonadism, selective estrogen receptor modulators (SERMs) and aromatase inhibitors have been studied for the treatment of hypogonadism. They are more often studied in infertile men because they enhance rather than inhibit gonadal function.

The most well studied SERM is clomiphene citrate, with most studies reporting an average increase in serum testosterone of 300 ng/dL. The mechanism of action is by attenuating the negative feedback of estrogen on the hypothalamus and pituitary, leading to an increase in LH. Thus, it is less likely to work in men with hypogonadism due to testicular failure.

An isomer of clomiphene citrate, enclomiphene citrate, is being evaluated by the FDA for treatment of hypogonadal men.

Aromatase inhibitors such as anastrazole and letrozole have also been studied as treatment for hypogonadism. Their mechanism of action is by inhibiting the conversion of testosterone to estradiol. Their use has been evaluated in infertile men and obese hypogonadal men, who have an altered testosterone to estrogen ratio due to the presence of aromatase in adipose tissue.

Since neither clomiphene citrate nor anastrazole is FDA approved for use in men, their adverse events are not well reported. A theoretical concern about worsening bone mineral density (from decreased estrogen levels or estrogen action) has led many experts to order a DEXA scan periodically in these men.

Human chorionic gonadotropin (hCG) also stimulates Leydig production of testosterone. It is administered either subcutaneously or intramuscularly and is expensive, so it is used less commonly than clomiphene citrate or anastrazole, which are oral and generic.

The patient decides that he would rather be treated with an exogenous form of testosterone.

What are the preparations available to prescribe?

1. Transdermal testosterone is available in multiple formulations
   a. A potential benefit of this preparation is a steadier state of serum testosterone
   b. Adverse events specific to this formulation include skin reactions and the potential for direct transfer to their partners or children
2. Intramuscular testosterone is administered into the quadriceps or gluteus muscles
   a. It is the most affordable method of testosterone replacement
   b. Injections should be administered approximately every week at a low dose (100 mg) to minimize the peak and trough effects seen with high doses injected less frequently
   c. It is associated with more variation in levels between doses, with a peak after administration and a trough before administration
   d. Testosterone undecanoate is a long acting form that is administered in the office every 10 weeks. It is only administered by physicians enrolled in a risk evaluation and monitoring system for pulmonary oil microembolism
3. Subcutaneous pellets are another long acting form that can be inserted into the flank or buttocks
   a. This approach leads to physiological levels that last approximately 3 months and are best used after a patient has demonstrated symptom improvement with other forms of testosterone supplementation first

   b. Adverse events include bruising (7%), infection (5%), pain (1%), and pellet extrusion (1%)

4. Buccal administration of testosterone is the only oral method available in the US and is applied to the upper gum. Adverse events are a bitter taste and some gum irritation

The patient elects transdermal testosterone.

In addition to monitoring his symptoms and serum testosterone, what other labs should you be monitoring?

1. Erythrocytosis is the most common adverse event with testosterone replacement therapy. You should evaluate a hematocrit at 3 months, 6 months, 12 months, and annually thereafter while a patient is on treatment
2. Additionally, PSA should be evaluated in men aged 40 and older at the same time intervals

He returns 3 months later complaining that he does not feel any better. His serum testosterone is 280 ng/dL, his hematocrit is unchanged at 43%, and his PSA is unchanged at 1.1 ng/mL.

Next step?

Ensure that the patient is applying the medication to clean, dry skin and is not washing off the drug. For men applying the medication properly, options include dose escalation, changing to a different transdermal formulation, or changing to a different mode of administration. Up to 20% of men respond suboptimally to one transdermal formulation and may respond to a different one.

The patient decides to use intramuscular testosterone instead. On IM testosterone, his peak level is 843 ng/dL, while his trough level is 480 ng/dL. At the patient's 6-month follow-up, his hematocrit is 56% and his PSA is 1.2 ng/mL, up from a baseline of 1.1 ng/mL.

Next step?

Evaluate for any sequelae of erythrocytosis, such as thrombosis. Treatment options are therapeutic phlebotomy and decreasing the dose. While not definitive, literature suggests that intramuscular testosterone (with its higher peaks), may increase the hematocrit more than other transdermal testosterone.

He undergoes therapeutic phlebotomy with a resulting hematocrit of 50%. You also reduce the dose of the medication. His peak and trough testosterone 3 months later are 712 ng/dL and 420 ng/dL respectively. His hematocrit is 50% and his PSA is 1.2 ng/mL. His symptoms remain improved.

His symptoms and labs are stable at his next visit in 6 months, but 8 months after initiation of intramuscular testosterone, he calls the office complaining of breast enlargement and tenderness.

Next step?

The patient has developed gynecomastia. You evaluate his testosterone and estradiol levels and find that they are 730 ng/dL and 62 pg/mL (normal level <40) respectively. Your options are to discontinue therapy or switch to alternative agents like clomiphene citrate or anastrazole. There is limited data that these alternative medications are less likely to result in gynecomastia.

CHAPTER 14

PEDIATRICS

ANJA ZANN, MD
ROMANO DEMARCO, MD

CASE 1

HPI: 2-day-old male with non-palpable right testis. The maternal history is unremarkable. No medications (esp. steroids) taken during pregnancy. Normal screening prenatal ultrasound performed at 20 weeks gestation. The pregnancy and delivery were uneventful; infant born at term. Apgar scores 9 and 9 at birth. Respiratory status normal. Infant has had multiple voids since birth.

PMH: none

PSH: none

Allergies: none **Medications:** none

FH: no family history of undescended testes
SH: lives with both parents
ROS: unremarkable

PE:

Vitals	T 98.4	BP 84/56	P 170	RR 34
GA	no distress; well-developed, well-nourished 2 day old			
HEENT	EOMI; PERRLA			
Heart	RRR			
Lungs	CTA B			
Abdomen	soft; non tender; no palpable masses			
Back	(-) dimple; (-) hairy patch			
GU	normal uncircumcised phallus; left testicle palpable in the scrotum; right testicle is non-palpable; normal scrotum			
Anus	normal position			
Ext	normal pulses and tone			
Neuro	normal spontaneous movement; no obvious neurologic deficits			

What laboratory tests do you order?

None.

What imaging tests would you order?

None, there is no imaging study that can reliably locate a non-palpable testis.

If the child also had a proximal hypospadias, how would your workup differ?

1. You would be concerned for a disorder of sexual development (DSD)
2. You would consider ordering:
   a. Karyotype
   b. MIS, LH, FSH, inhibin B, and testosterone levels

What is your assessment and recommendation for this patient?

Newborn male with right non-palpable testis.

Re-evaluate in 4 months.

He returns in 4 months with an unchanged exam. What do you recommend?

Discuss the recommendations for surgery:

1. Unlikely that spontaneous descent will happen after 6 months
2. Surgery ideally done by 18 months to preserve fertility potential

IMPORTANT: Because of its limited efficacy, hormonal therapy is NOT recommended.

Mother of child asks: "Is it necessary to do surgery? What are the risks of observation?"

1. Malignancy
   a. Relative risk is 2.75
   b. This risk is reduced following pre-pubertal orchiopexy
2. Infertility
   a. The duration of time the testis is undescended and higher the position of the testis at time of orchiopexy seems to correlate with higher rates of germ cell loss and risk of infertility
3. Paternity rates:
   a. 65% for former bilateral UDT patients who had surgery
   b. 90% for former unilateral UDT patients who had surgery
   c. 93% for control male without UDT

What are important points to discuss during the informed consent process?

Possible staged procedure, need for orchiectomy, injury to testis and vas deferens, and testicular atrophy occurring over time following surgery.

Discuss surgical technique:

1. Exam under anesthesia to determine if testicle is palpable
2. If testis is palpable:
   a. Inguinal orchiopexy
      i. Inguinal incision; locate testis; transect gubernaculum distal to hernia sac; isolate hernia sac off spermatic cord and ligate at the level of the internal ring; division of all spermatic fascial attachments
      ii. Scrotal incision with subdartos pouch and testis fixation
3. Non-palpable testis: diagnostic laparoscopy
   a. What are you looking for once you have camera access?
      i. Presence of testis and its relation to the ipsilateral internal ring
      ii. Atretic internal spermatic vessels extending inferiorly to a closed internal ring is consistent with a vanishing testis; no further surgery required
      iii. Length of vas deferens. If vas deferens is short, it will make orchiopexy difficult as short vas will tether testis
4. Surgical options for intra-abdominal testis:
   a. Primary laparoscopic orchiopexy
      i. Use if testis is approximately < 2 cm from ipsilateral internal ring
      ii. 2, 3 or 5 mm laparoscopic instruments are used to mobilize and free spermatic cord to gain cord length for transfer into scrotum
   b. Fowler-Stephens laparoscopic orchiopexy
      i. Used when testis is in a high intra-abdominal position (>2 cm above the internal ring)
      ii. Internal spermatic vessels are divided to gain length and blood supply to testis is based on the deferential artery and collateral peritoneal vessels

   iii. 1 stage procedure involves transecting spermatic vessels and positioning testis in scrotum in one surgery
   iv. 2 stage procedure involves placing occlusive clips on internal spermatic vessels with little manipulation of testis. Return in 6 months to divide internal spermatic vessels and position testis in the scrotum. Thought to have higher success rate as compared to 1 stage procedure as it allows for more robust collateral blood vessel development prior to scrotal positioning

Assuming the contralateral testicle is normal, what are indications for orchiectomy at the time of exploration?

1. Hypoplastic or dysmorphic testicle
2. Short vas deferens
3. Post-pubertal age

What is postoperative follow-up after orchiopexy?

1. 1 and 6 month post-operative check of the size, consistency, and location of the testis
2. Recommend annual testicular exam by PCP

What are the success rates following orchiopexy?

1. >95% for inguinal orchiopexy
2. 70–90% for 1 or 2 stage Fowler-Stephens orchiopexy

An 8-year-old boy returns to your office after having a left inguinal orchiopexy at 1 year of age. His right testis is palpably normal. His left testis is faintly palpable in the left hemiscrotum. What is your next step?

1. If you are certain that testis is in scrotum but atrophic, then observation
2. If you think that the testis has retracted out of the scrotum, then redo orchiopexy or possible orchiectomy

Related questions

Describe testicular descent:

1. Phase 1: Transabdominal
   a. First trimester
2. Phase 2: Inguinoscrotal
   a. Occurs at 25–30 weeks
   b. Androgen dependent

How common is cryptorchidism?

1. Birthweight <900 g: ~100%
2. Birthweight 2,700–3,600 g: ~ 3%
3. Premature: ~15–30%
4. Term: ~ 1–3%
5. In all boys ~1% will require surgery for UDT

How should retractile testes be managed?

1. Annual exam to check for location
2. Rarely will ascend and require orchiopexy

CASE 2

HPI: A newborn male infant in the nursery is found to have hypospadias. Maternal history unremarkable. No medications were taken during pregnancy. Pregnancy and delivery were uneventful. Infant born at term. Mother has 2 sons and 1 daughter. Father has history of hypospadias corrected as a child. No prenatal ultrasound was done. Normal amniotic fluid present at birth. Apgar scores 9 and 9. Infant seen voiding spontaneously. Normal respiratory status.

PMH: none

PSH: none

Allergies: none **Medications:** none

FH: father with hypospadias
SH: lives with both parents and 3 older siblings
ROS: none

PE:

Vitals	T 98.6	BP 82/60	P 160	RR 36
GA	healthy appearing newborn infant			
HEENT	benign			
Heart	RRR			
Lungs	CTA			
Abdomen	soft; NT/ND			
Back	(-) dimple; (-) hairy patch			
GU	uncircumcised phallus; hypospadiac meatus located proximal to the coronal sulcus; dorsal hood; mild ventral chordee; penile stretch length is 3.5 cm; testes descended and palpably normal; scrotum well developed			
Anus	normal anatomic position			
Ext	(-) CCE			
Neuro	non-focal			

What laboratory tests do you order?

No laboratory studies are indicated.

Does this infant need karyotype or hormonal studies?

No. Obtain karyotype testosterone, FSH and LH in patients with:

1. Perineal hypospadias
2. UDT with proximal hypospadias
3. Additional major congenital anomaly
4. Concerns for DSD

What is your assessment?

Newborn male with distal hypospadias. No evidence of ambiguous genitalia.

Does he need any imaging studies?

No.

When are imaging studies considered?

Boys in which there is a concern for a DSD or those with syndromic hypospadias.

What studies are typically ordered in patients where there is a concern for a DSD?

Pelvic ultrasound and genitogram.

What is your recommendation?

1. Perform hypospadias repair at 6–12 months of age as advocated by the American Academy of Pediatrics
    a. Boys have significant phallic growth around 3 months of age due to testosterone surge around 2 months of age
2. Because of cognitive, developmental and emotional factors, pediatric urologists in general recommend hypospadias surgery to be completed by 15 months of age

What are the risk factors for hypospadias?

1. Heredity: 10% of boys with hypospadias have an affected relative
2. Endocrine disruptors: concern that natural or synthetic compounds exerting estrogen-like or anti-androgen effects may lead to hypospadias
3. Fetal endocrinopathies which alter testosterone production or its action
4. Over 200 syndromes are associated with hypospadias

Where are the different locations of the meatus in hypospadias?

1. Glanular/coronal	70–80%
2. Shaft	10–20%
3. Penoscrotal	3–5%
4. Perineal	≤ 1%

When would you proceed with a work-up for a DSD in a child with hypospadias?

1. In newborn with severe hypospadias and nonpalpability of 1 or both testes
2. Most common DSD in a boy is mixed gonadal dysgenesis (MGD). Patients with this condition have a 45,X/46,XY mosaicism with ambiguous genitalia, a unilateral UDT (typically intra-abdominal), and a contralateral streak gonad
3. Female neonates with congenital adrenal hyperplasia (CAH) can present with a masculinized clitoris very similar to a boy with severe chordee and a proximal hypospadias

When would one consider preoperative testosterone stimulation?

1. In boys with small penises and/or small glans penis—increase penile and glans size
2. In boys with significant ventral chordee—reduce severity of chordee
3. Re-operative hypospadias surgery to increase size of penis and improve vascularity to penile tissues
4. Administration can be either topical or parenteral, usually started 4–6 weeks prior to surgery. Intramuscular injection usually given typically as 2–3 injections

What are the desired outcomes following hypospadias surgery?

1. Cosmetically normal appearing phallus, either circumcised or with foreskin reconstruction
2. Normal caliber neourethra with urethral meatus located in glans
3. Straight phallus

The child returns to your office at 10 months of age and parents desire surgery.

How do you proceed?

State that you would obtain informed consent. Potential complications include urethral stricture, meatal stenosis, urethrocutaneous fistula formation, persistent chordee, and penile skin breakdown.

What are the key steps when doing a hypospadias repair?

1. Correction of congenital penile curvature
2. Urethroplasty
3. Interposition of tissue barrier between the neourethra and skin closure
4. Glansplasty
5. Skin closure including circumcision or foreskin reconstruction

Hypospadias Repair—general principles

1. Circumferential incision
2. Carry the incision proximal to the meatus
3. Preserve the urethral plate (ventral penile skin distal to the meatus)
4. Deglove the penis
5. Artificial erection with preservative free saline to assess for presence of chordee

Chordee Repair

1. Deglove the penis down to the penopubic and penoscrotal junction
2. If persistent curvature exists following penile degloving of <30°: Perform dorsal plication in the midline avoiding neurovascular bundles, which are located at the 1 and 11 o'clock positions
3. If curvature exists after placement of dorsal plication suture or the curvature is >30° after degloving, mobilize urethra plate off the corporal bodies and repeat artificial erection
4. If curvature persists, transect the urethral plate off the corporal bodies at the corona or at the junction of normal urethra. Make a transverse incision through the tunica albuginea ventrally at the point of maximal curvature in the corporal bodies from the 3 to 9 o'clock position. Then graft the defect with either dermis, single-ply small intestinal submucosa (SIS), or with a tunica vaginalis flap

Urethroplasty options for primary hypospadias:

1. Distal (from distal shaft into glans)
   a. Tubularized incised plate (TIP) repair (most commonly used)
   b. Tubularization techniques without incising plate:
      i. Thiersch-Duplay technique
      ii. Mathieu (flip-flap) repair
   c. Urethral advancement
2. Proximal (from penoscrotal position to mid-shaft)
   a. TIP repair

- b. Preputial skin flap
  - i. Onlay technique
  - ii. Koyanagi technique
- c. 2-stage repair. Second stage performed 6–12 months following first surgery
  - i. Using Byars' preputial flap
  - ii. Buccal graft

Describe flaps used to cover neourethra to minimize risk of fistula formation.

1. Local flap of periurethral dartos fascia
2. Rotation of dorsal or preputial dartos flap
3. Tunica vaginalis flap (from scrotum)

A TIP repair was performed uneventfully. The child develops urine leakage at the operative site 2 weeks later.

What is your assessment and plan?

1. He has developed a urethrocutaneous fistula
2. You need to wait at least until 6 months before a correction is attempted

What are complications of hypospadias repair and management?

1. Urethrocutaneous fistula
   - a. The longer the urethroplasty, the higher the rate of fistula
   - b. Most common at the junction of native urethra and the neourethra
   - c. Wait at least 6 months for surgery to allow in-growth of vascular supply and full resolution of edema
2. Urethral stricture
   - a. Occurs at proximal or distal ends of anastomosis
   - b. Treat with urethral dilation, DVIU, or urethroplasty
3. Meatal stenosis
   - a. Trial of corticosteroid cream then meatoplasty if persists
4. Urethral diverticulum
   - a. Due to distal obstruction or elastic skin used in initial repair
   - b. Correct distal obstruction and excise redundant skin, or consider completely resecting skin used for urethra and performing buccal staged urethroplasty

CASE 3

HPI: A newborn infant is born is with ambiguous genitalia. Maternal history is unremarkable. No drug ingestion during pregnancy. Pregnancy and delivery were uneventful. No urologic problem with other children in family. No family history of genital or genetic disorders or issues with infertility. No prenatal ultrasound done. Apgar scores 9 and 9. Infant is tachypnic. Infant appears dehydrated and not feeding well. Infant has voided.

PMH: none

PSH: none

Allergies: none **Medications:** none

FH: mother has issues with recurrent kidney stones
SH: lives with both parents and 2 older siblings
ROS: unremarkable

PE:

Vitals	T 98.6 BP 76/48 P 180 RR 54
GA	sickly appearing newborn infant
HEENT	normal
Heart	RRR
Lungs	CTA
Abdomen	soft; NT/ND; (-) masses
Back	(-) dimple; (-) hairy patch
GU	small phallus with severe ventral chordee; testes not palpable; meatus visualized with bifid scrotum at penoscrotal junction
Anus	normal anatomic position
Rectal	feel a mass anteriorly
Skin	hyperpigmentation of areola and labia
Extremities	normal muscular tone; normal pulses
Neuro	normal

What are the key findings on physical examination?

1. Stretched penile length and diameter of the phallus
2. Severity of congenital curvature
3. Location of the urethral meatus
4. Palpability and size of testes
5. Size and appearance of the scrotum
6. General size and appearance of the clitoris. In patients with significant clitoromegaly, a stretched length and width should be taken
7. Location of the meatus and relationship to separate vaginal orifice
8. Presence of both urethral and vaginal opening. In female fetuses exposed to high levels of testosterone in-utero, a common distal stem off the vagina and urethra can occur (urogenital sinus)
9. Appearance of labia. Fusion, anterior placement of the labia with hyperpigmentation, and absence of the labia minor are signs of in-utero androgen exposure
10. Uterus may be palpable on rectal exam as cord-like structure anterior to rectum

When should an evaluation for a disorder of sexual differentiation proceed?

1. Overt genital ambiguity
2. Apparent female genitalia with an enlarged clitoris, posterior labial fusion, or an inguinal or labial mass
3. Apparent male genitalia with bilateral undescended testes, micropenis, isolated perineal hypospadias, or hypospadias with non-palpable testis

What laboratory study should be sent immediately?

Basic metabolic profile.

Laboratory values are:

BMP → Na 126 meq/L; K 5.8 meq/L; Cl 100 meq/L;
CO 24 meq/L; glucose 110 meq/L;
BUN 10 mg/mL; Cr 1.3 mg/dL

What is your next step?

Resuscitate the infant with intravenous fluids and correct the electrolyte abnormalities.

What else would you highly recommend?

Involve a group of physicians from neonatology, endocrinology, medical genetics, and psychiatry/psychology who have experience in managing neonates and their families in situations where a DSD is suspected.

What other laboratory studies would you order?

1. Testosterone level
2. Serum 17-hydroxyprogesterone level
3. Karyotype

What initial imaging studies would you order?

Abdominal and pelvic ultrasound.

1. The presence of a uterus is accurately seen with pelvic ultrasound
2. Gonads may be seen but specificity and sensitivity of ultrasound is poor for non-palpable testes and presence of ovaries
3. In experienced hands, adrenal sonography is an accurate adjunct in making the diagnosis of congenital adrenal hyperplasia (CAH)

The laboratory values and sonogram return these results:

1. Testosterone levels are elevated
2. 17-OH progesterone levels are markedly elevated
3. Karyotype 46,XX
4. A uterus is seen on the ultrasound

What is your diagnosis?

Congenital adrenal hyperplasia (CAH)

1. CAH is the most common DSD in general
2. 3 enzymatic defects cause CAH. 21-hydroxylase is by far the most common and is responsible for 95% of cases of CAH. This enzyme catalyzes the conversion of 17-OH progesterone to 11-deoxycortisol
3. There are 2 forms of 21-HD deficiency. The most common classic presentation is an infant with both salt wasting and virilization (75%)
4. Salt wasters have symptoms of nausea, vomiting, dehydration, and progressive weight loss. Without rapid and appropriate resuscitation, death can occur due to hyperkalemia and shock
5. 11β-hydroxylase deficiency is the second most likely enzymatic defect leading to virilization in patients with CAH. Patients have marked virilization but in contrast typically have hypertension due to the increased serum levels of deoxycorticosterone

What is your next step?

Start glucocorticoid (hydrocortisone) and mineralocorticoid (fludrocortisone) after discussion with Pediatric Endrocrinology.

The infant responds nicely to medical therapy. She is thriving, and there appears to be some reduction in the size of her clitoris.

Infant's parents ask what is the timing of surgery and if any other studies need to be done prior?

What is your response?

1. You discuss with the parents that based on multiple factors, genital surgery is best performed around 2–6 months of age
2. You recommend a preoperative genitogram to determine the length of both the confluence of the common urogenital sinus and urethra off the sinus
3. You also discuss the need for stress corticosteroid dosing perioperatively

Describe the surgical approach.

1. Start with endoscopy to assess the child's internal genital and urinary tract findings
2. A feminizing genitoplasty is performed to reduce the size and appearance of the clitoris, reconstruct the clitoral skin, and reshape the labia majora and minora
3. For those girls with a low confluence a flap vaginoplasty is the best approach. For those patients with a higher confluence, a urogenital mobilization procedure is typically the best option

You perform surgery and the child does well. On postoperative follow-up she is noted to void without issue, and her cosmetic appearance is good. You do not see her for years, but presents at age 13 with cyclical pain and only spotting during her period. She is not able to place a tampon into her vagina. On physical examination she has scarring of her vaginal introitus with a pinpoint opening present.

What is your primary concern?

Vaginal stenosis.

You recommend a redo vaginoplasty and close follow-up after surgery as she gets older to make sure sexual intercourse is satisfactory

Change only the scenario of the laboratory results to the following:

1. Testosterone levels are normal
2. 17-OH progesterone levels are normal
3. Karyotype 45,XO/46,XY
4. An apparent small uterus is seen on ultrasound

What is your diagnosis?

Mixed gonadal dysgenesis (MGD) [46,XY DSD]. It is the second most common cause of a DSD.

MGD is a group of disorders characterized by a unilateral testis, which is typically undescended, an intraabdominal contralateral streak gonad, persistent mullerian duct structures, and varying degrees of virilization of the external genitalia.

Other DSD conditions:

1. Ovotesticular DSD (formerly known as true hermaphroditism)
    a. Defined as an individual who has both testicular and ovarian tissue
    b. Most of these patients are raised as males after hypospadias and chordee repair
    c. If raised as female, all Wolffian and testicular tissue should be excised
    d. If raised as male, all mullerian and ovarian tissue should be excised
    e. If ovotestis present, surgical cleavage of the gonad can be performed
2. Androgen sensitivity syndromes
    a. Abnormalities of androgen receptor function represent the most common definable cause of the undervirilized male and are transmitted as an X-linked trait
    b. Complete androgen insensitivity (previously known as testicular feminization) is characterized by a 46,XY karyotype, bilateral undescended testes, female-appearing external genitalia, and absence of mullerian structures
    c. Patients with complete androgen insensitivity have a female appearance and commonly present as adolescents with amenorrhea, absence of pubic hair, and with inguinal hernias containing testes
    d. Newborns with partial androgen insensitivity have incomplete masculinization of their external genitalia and most commonly present with hypospadias, bilateral undescended testes, and rudimentary Wolffian structures
3. Disorder of androgen action
    a. 5α-reductase is an enzyme which converts testosterone to dihydrotestosterone
    b. Boys have normal formation of testes and male internal ducts through the action of testosterone
    c. However, without conversion to dihydrotestosterone, normal external genitalia formation does not occur
    d. Neonates present with ambiguous genitalia or with severe hypospadias
4. Persistent mullerian duct syndrome (formerly known as hernia uteri inguinale)
    a. These patients have a 46,XY karyotype and normal male external genitalia with either unilateral or bilateral undescended testes with fallopian tubes, a uterus and upper vagina which drains into a prostatic utricle
    b. Thought to be due to abnormality in the gene, which is involved in the production of mullerian inhibiting substance (MIS)
    c. The vas deferens are in close proximity to the mullerian structures and complete excision of these structures is only recommended if it can be done safely

When is prophylactic gonadectomy or removal of streak gonads generally recommended?

In patients raised as girls with Y genetic material.

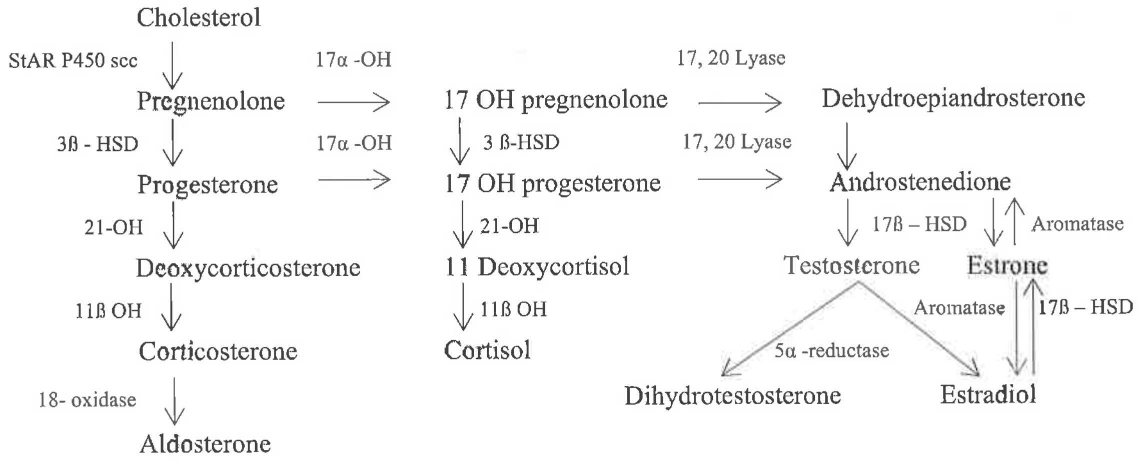
What are the most common gonadal tumors associated with DSD?

Gonadoblastoma and dysgerminoma.

Classification of Disorders of Sexual Differentiation (DSD):

1. Sex chromosome disorders of sex development
    - a. 45,X/46,XY (Mixed gonadal dysgenesis)
    - b. 47,XXY (Klinefelter syndrome and variants)
    - c. 45,X (Turner syndrome and variants)
    - d. 46,XX/46,XY (Chimerism or ovotesticular disorder)
2. 46,XY Disorders of sex development
    - a. Disorders of testicular development
        - i. Complete gonadal dysgenesis
        - ii. Partial gonadal dysgenesis
        - iii. Testis regression syndrome and Bilateral Vanishing Testes Syndrome
    - b. Disorders in androgen synthesis or action
        - i. Androgen biosynthesis defect
        - ii. Androgen receptor and postreceptor defects
            - aa. Androgen insensitivity syndromes
            - bb. Disorder of androgen action
        - iii. Luteinizing hormone receptor abnormality
        - iv. Anti-mullerian hormone and receptor abnormality
3. 46,XX Disorders of sex development
    - a. Disorders of ovarian development
        - i. Gonadal dysgenesis
        - ii. Testicular disorder of sex development (46,XX male)
        - iii. 46,XX ovotesticular disorder
    - b. Androgen excess
        - i. Congenital adrenal hyperplasia
        - ii. Maternal excess
4. Other conditions
    - a. Cloacal exstrophy
    - b. Hypospadias

Steroid Biosynthetic Pathway



CASE 4

HPI: 32-year-old female G3P2 referred to you for postnatal management of fetal right sided hydronephrosis found on prenatal ultrasound. Prenatal sonography at 18 weeks found mild right hydronephrosis. The left kidney and bladder were normal. There was no oligohydramnios present. Repeat fetal sonography at 32 weeks post-conceptual age is normal except for worsening, now moderate right hydronephrosis.

What do you recommend for follow-up?

Postnatal renal-bladder (RBUS) ultrasound be performed 24–48 hours after birth.

A few months later you receive a call from the pediatric service from the nursery that your patient's child has been born via a term, vaginal delivery without issues. The baby appears healthy. A renal ultrasound immediately after birth demonstrated no hydronephrosis. The pediatricians ask you if anything further needs to be done since the ultrasound was normal.

Does the ultrasound need to be repeated?

YES. Neonates are often dehydrated shortly after birth and resolution of hydronephrosis on ultrasound may be a false negative.

You explain that the ultrasound needs to be repeated in 24–48 hours, and you go to evaluate the infant.

PMH: none

PSH: none

Allergies: none. **Medications:** none

FH: mother with history of hydronephrosis which resolved as infant
SH: lives with both parents and 2 older brothers
ROS: unremarkable

PE:

Vitals	T 98.4	BP 84/58	P 160	RR 22
GA	no distress, well-developed, well-nourished newborn male			
HEENT	EOMI, PERRLA			
Heart	RRR			
Lungs	CTA B			
Abdomen	soft, non-distended, RUQ firm mass			
GU	normal appearing uncircumcised penis; both testes palpably normal and descended; normal scrotum			
Back	(-) dimple; (-) hairy patch			
Anus	normal position			
Ext	normal pulses; normal tone			
Neuro	normal			

A repeat RBUS on day of life 2 shows moderate right hydronephrosis. There is no ureteral dilation. The left kidney and bladder are normal.

What is your differential diagnosis at this point, and what do recommend next?

Right hydronephrosis secondary to UPJ obstruction or VUR. Less likely diagnoses include an ectopic ureter (absence of ureteral dilation), ureterocele (absence of ureteral dilation and cystic structure present in bladder on ultrasound), or posterior urethral valves (unilateral issue, no ureteral dilation, and normal appearing bladder).

What additional testing would help differentiate between the possible diagnoses?

VCUG and nuclear renogram.

The infant is going to be discharged home to follow up with you in 2 weeks after VCUG and nuclear renogram are performed.

Is there anything else you want to recommend before discharge?

Yes. Antibiotic prophylaxis should be recommended until VUR is excluded with VCUG.

Results show:

1. A normal bladder and urethra without evidence of reflux is seen on VCUG
2. The MAG3 nuclear renogram demonstrates:
    a. Good split function bilaterally
    b. Left T ½ of 10 minutes
    c. Right T ½ calculated to be 80 minutes

Now what is your assessment?

2-week-old with right UPJ obstruction with normal functioning kidneys.

What is your recommendation?

Surgical intervention with open dismembered pyeloplasty.

What are the different surgical options, and what are the indications/contraindications of each?

1. Dismembered pyeloplasty (Anderson-Hynes technique). Standard method
    a. Allows for excision of the abnormal UPJ section, renal pelvic reduction and transposition of crossing vessel (if present)
    b. Contraindicated in patients with long proximal ureteral stricture
    c. Approach: anterior subcostal, flank, or dorsal lumbotomy
    d. Identify renal pelvis and expose UPJ
    e. Transect and excise UPJ
    f. Spatulate ureter laterally and excise redundant renal pelvis
    g. Anastomosis performed using fine interrupted or running suture
    h. Place indwelling stent or nephrostomy tube
    i. Leave perirenal drain
2. Foley Y-V plasty
    a. Good for high inserting ureter or horseshoe kidney

   b. Contraindicated if need for transposition of crossing vessel or need for pelvic reduction
3. Spiral flap (Culp-DeWeerd)
   a. Good for pelvic reduction or long proximal ureteral stricture
   b. Contraindicated if need for transposition of crossing vessel
4. Vertical flap (Scardino-Prince)
   a. Good for pelvic reduction or medium length proximal ureteral strictures
   b. Contraindicated if need for transposition of crossing vessel

Mother asks about the option of laparoscopic robotic-assisted surgery.

What do you discuss with her?

1. The small working space present in children limits the use of laparoscopic robotic-assisted surgery until at least 6 months of age
2. With an experienced minimally invasive surgeon, the length of surgery and operative results are comparable to an open pyeloplasty

What are other presenting signs and symptoms of a UPJ obstruction in a child?

1. Episodic flank or upper abdominal pain
2. Cyclical nausea and vomiting
3. Azotemia (unlikely if contralateral kidney normal)
4. Kidney stones
5. Pyelonephritis

What would be indication for nephrectomy?

Massive hydronephrosis in poorly functioning kidney (<15%).

You perform a dismembered pyeloplasty without complication and he has excellent outcome.

What is your plan for follow-up?

RBUS in 1–2 months after stent or nephrostomy tube removed.

If hydronephrosis is seen on initial postoperative ultrasound RUS, what do you recommend?

1. Repeat RBUS in 1–2 months. It is very common to see hydronephrosis on early postoperative imaging, which typically improves over time
2. If the hydronephrosis on postoperative imaging does not improve you would recommend a nuclear renogram to assess renal function and drainage

Postoperative imaging demonstrates a recurrence of the UPJ obstruction following pyeloplasty.

What do you recommend?

As long as there is reasonable renal function (>15%) in the affected kidney, a redo pyeloplasty, spiral or vertical flap procedure, or ureterocalicostomy.

What are the most common causes UPJ Obstruction?

1. Instrinsic
    a. Attenuated and separated muscle fibers with increased collagen deposition at the UPJ which leads to insufficient emptying of the renal pelvis (most common cause)
    b. Valvular mucosal folds
    c. Ureteral polyps
    d. Persistent fetal convolutions
2. Extrinsic
    a. Crossing vessel (over the lower pole)

What are the associated anomalies in the GU system with UPJO?

1. UPJO of the contralateral kidney (10–40%)
2. VUR of both contralateral and ipsilateral kidney
3. Multicystic dysplastic contralateral kidney
4. Duplicated system with UPJ obstruction almost exclusively found in lower pole moiety
5. VATER syndrome (Vertebral defects, Imperforate anus, Tracheoesophageal fistula, and Radial and Renal dysplasia)

CASE 5

HPI: 2-month-old girl presents with fever and malodorous urine. Maternal history unremarkable. Pregnancy and delivery were uneventful; infant born at term. No urologic problems in family. Prenatal ultrasound was not done. No other children in family.

PMH: none

PSH: none

Allergies: none **Medications:** none

FH: none
SH: lives with both parents
ROS: no respiratory or GI problem

PE:

Vitals	T 101.6 BP 78/44 P 174 RR 32
GA	lethargic appearing F infant
HEENT	benign
Heart	sinus tachycardia
Lungs	CTA
Abdomen	soft; NT/ND; (+) suprapubic mass
Back	(-) dimple; (-) hairy patch
GU	normal external female genitalia
Anus	normal anatomic position
Ext	normal pulses; normal tone
Neuro	normal

What initial lab tests do you order?

UA/microscopy → many WBCs; TNTC bacteria
UCx → pending (will grow out Klebsiella; pansensitive)
Chem 7 → normal electrolytes; creatinine 0.4 mg/dL
WBC → 15,900 (60% neutrophils/8% bands)
BCx → pending

How would you obtain a urine sample?

1. Sterile urethral catheterization is the best method
2. Suprapubic aspiration is the next best method if unable to collect sterilely by urethral catheterization
3. Bag collection is not recommended as this method has a high rate of contamination

She was catheterized and a total of 95 mL of urine was obtained.

Is this normal?

No. Expected bladder capacity can be calculated using one of these 2 formulas:

1. Age: Age (in years) + 2 = urine capacity in ounces
   $(0 + 2 = 2 \text{ ounces} \times 30 \text{ mL/ounce} = 60 \text{ mL})$

2. Weight in infancy: Weight (in kg) × 7 = urine capacity
   (6.0 kg × 7 mL/kg = 42 mL)

What do you do next?

Fluid resuscitate with IVFs and start broad spectrum antibiotic coverage (Ampicillin and Gentamicin).

What is your differential diagnosis?

1. Ureterocele acting as a ball-valve obstructing the bladder neck
2. Neurogenic bladder with urinary retention

What initial radiographic studies would you order?

Renal and bladder ultrasound.

Renal ultrasound:	left upper pole hydronephrosis with findings suggestive of a duplicated collecting system; dilated left upper pole ureter seen down to level of bladder; normal left lower pole and right kidney
Bladder US:	distended bladder, cystic mass within the bladder; dilated left ureter seen behind bladder

What is your assessment?

1. She most likely has an intravesical left ureterocele that prolapses into the urethra with voiding and impairs bladder emptying
2. A ureterocele is rarely seen as a congested intralabial mass on physical examination

What do you do next?

Place feeding tube or small Foley catheter to decompress her bladder.

She remains febrile and lethargic after 24 hours of bladder decompression.

What do you recommend?

Decompression and drainage of obstructed system with either:

1. Transurethral incision of left ureterocele
2. Percutaneous nephrostomy tube placed in left upper pole

How do you proceed?

You proceed with transurethral incision.

Discuss your technique for incising the ureterocele.

1. Use pediatric resectoscope (9–11 Fr) or pediatric cytoscope (7–10 Fr) with a Bugbee electrode, angle wire, or holmium laser
2. Make a 2–4 mm transverse incision at the lowest point of the ureterocele within the bladder and ensure drainage with visualized jet of urine emanating from ureterocele

3. If the ureterocele extends into the urethra, a second incision should be made at the lowest point of the ureterocele within the urethra to prevent obstruction due to "windsock" creation

She underwent transurethral incision of the ureterocele. Her fever resolves and her clinical status improves.

What is the incidence of ipsilateral VUR after transurethral incision of ureterocele?

1. 0–50% with success dependent on location of ureterocele and technique. Ectopic ureteroceles have much higher rate of denovo VUR after incision
2. VUR more commonly found in lower pole ureter

What additional imaging studies would you obtain?

State that you would obtain a VCUG and nuclear renogram while on prophylactic antibiotics. A repeat RBUS can be helpful to confirm adequate decompression of ureterocele.

RBUS:	Left upper pole hydronephrosis persists, but left lower pole ureteral dilation improves. Bladder demonstrates decompressed left ureterocele
VCUG:	(-) vesicoureteral reflux, no ureterocele visible
Nuclear renogram:	normal function of (R) kidney and (L) lower pole moiety; non-function of (L) upper pole moiety

What is your assessment?

2-month-old female post status incised left ureterocele with non-functioning left upper pole moiety.

Note: When dealing with duplicated collecting systems, it is helpful to draw the anatomy on a piece of paper.

What are your options?

1. Left upper pole heminephrectomy with subtotal ureterectomy
2. Observation with serial ultrasounds to document resolution of the left upper pole hydronephrosis and continued decompression of the ureterocele
3. Common sheath re-implantation of the left upper and lower pole ureters; excision of the decompressed ureterocele in bladder; posterior bladder wall reconstruction or marsupialization of the ureterocele to the bladder mucosa

Parents choose to proceed with upper pole heminephrectomy.

Discuss your surgical technique for left upper pole heminephrectomy with subtotal ureterectomy.

1. Flank position with extraperitoneal exposure
2. Upper pole heminephrectomy with partial ureterectomy. Careful to ligate only vessesls feeding upper pole
3. Distal ureteral stump is left open and not ligated if there is no VUR

Following the heminephrectomy there is significant drainage from the perirenal penrose drain.

What is your next step?

Check fluid for creatinine and BUN level, while simultaneously checking a serum BMP to determine if fluid is urine.

The fluid comes back consistent with urine. What do you recommend?

Observation as long as child is acting well.

The drainage persists. What do you do next?

Order RBUS to:

1. Assess size of urinoma
2. Evaluate for presence of new onset hydronephrosis of the lower pole

On ultrasound there is no urinoma or hydronephrosis seen. You recommend observation.

The drainage tapers off over the next week, and you remove the drain. The child does well postoperatively on follow-up.

Related Information

How long does it take for newborn neonates to void?

Neonates usually void within the first 24 hours.

What is a normal creatinine level for a healthy newborn?

Normal creatine is <0.4 mg/dL after approximately 3–5 days of life in healthy term child. Prior to this, serum creatinine reflects maternal renal function.

When possible, how old should a child be when ordering a nuclear renogram?

If possible it is best to wait at least until the child is 3 months of age to perform a renogram. Prior to 3 months, the neonatal kidney is functionally immature and renography is not as accurate.

What does it mean if serum creatinine level does decrease to less than 1 mg/dL by 1 year of age?

If the creatinine is < 1 ng/mL by age 1 year, the risk for ESRD in childhood is high.

CASE 6

HPI: 6-week-old girl with fever and malodorous urine. Prenatal ultrasound revealed left upper pole hydroureteronephrosis. Normal right fetal kidney. Bladder was not distended. Normal amniotic fluid was seen. Pregnancy and delivery were uneventful; infant born at term. Maternal history unremarkable. Nourologic problems in family. No other children in family.

PMH: none

PSH: none

Allergies: none **Medications:** none

FH: none
SH: lives with both parents
ROS: unremarkable

PE:

Vitals	T 102.6	BP 82/58	P 170	RR 34
GA	lethargic appearing F infant			
HEENT	benign			
Heart	sinus tachycardia			
Lungs	CTA			
Abdomen	soft; NT/ND; LUQ mass			
Back	(-) dimple; (-) hairy patch			
GU	normal external female genitalia			
Anus	normal anatomic position			
Ext	normal pulses; normal tone			
Neuro	normal			

What initial laboratory tests do you order?

UA → many WBCs; TNTC bacteria; (-) proteinuria
UCx → pending (will grow out E. coli; pansensitive)
Chem 7 → normal electrolytes; creatinine 0.3 mg/dL
WBC → 13,200 (62% neutrophils/7% bands)
BCx → pending

What do you do first?

Resuscitate with IVFs and start broad spectrum IV antibiotics (ampicillin and gentamicin).

What is your differential diagnosis?

Pyelonephritis with history of prenatal left hydroureteronephrosis.

Differential diagnoses include:

1. Vesicoureteral reflux
2. UVJ obstruction
3. Ureterocele with obstructed upper pole hydroureteronephrosis
4. Ectopic ureter with hydroureteronephrosis

What initial radiographic studies would you order?

Obtain RBUS.

Renal ultrasound: severe left upper pole hydronephrosis with a dilated ureter coming off the upper pole; mild left lower pole hydronephrosis with no associated dilated ureter; normal right kidney

Bladder US: normal appearing bladder with moderately dilated left ureter seen behind the bladder

What is your assessment?

Severe left upper pole hydroureteronephrosis and mild left lower pole hydronephrosis. Concerning for an ectopic left upper pole ureter or ureterocele.

What do you do next?

Place indwelling catheter to decompress her bladder and continue the broad spectrum antibiotics until the urine culture and sensitivities are final.

The child responds well to treatment.

What additional imaging studies would you obtain?

Obtain a VCUG and nuclear renogram in the hospital on appropriate antibiotics after susceptibilities return or as an outpatient with the child on prophylactic antibiotics.

VCUG: no VUR in right kidney; grade 4 left lower pole VUR with no VUR seen in left upper pole; normal bladder and urethra

Nuclear renal scan: normal function of the right kidney; mild decrease in function of the left upper pole moiety with normal function of the left lower pole moiety; drainage curve of the right kidney and left lower pole moiety are normal; sluggish drainage initially seen in the left upper pole moiety but responds to Lasix with a T ½ of <15 minutes

What is your assessment?

6-week-old female with left hydroureteronephrosis of the upper pole secondary to an ectopic ureter and left lower pole grade 4 VUR.

Note: When dealing with duplicated collecting systems, it is helpful to draw the anatomy on a piece of paper.

What do you recommend as the next step?

1. Continued prophylactic antibiotics
2. Repeat RBUS in 3 months

Describe the Meyer-Weigert rule.

1. When there are 2 developing ureteral buds incorporating into the urogenital sinus, the most inferior bud which is associated with lower pole of the kidney is incorporated first and migrates more laterally (more prone to VUR)
2. The upper pole ureter is higher and is incorporated later and is more medial and inferior in location (more prone to obstruction)

The child returns to your clinic in 3 months. She has been doing well at home on prophylactic antibiotics with no issues with UTIs. A repeat RUS demonstrates no change in her severe left upper pole hydroureteronephrosis and mild lower pole hydronephrosis.

What do you recommend as the next step?

1. Continued prophylactic antibiotics
2. Repeat RBUS, VCUG, and nuclear renogram in 6 months

The child returns in 6 months doing well on the prophylactic antibiotic regimen. Repeat RUS, VCUG, and nuclear renogram are all unchanged.

What do you recommend as the next step?

Left common sheath ureteral reimplantation as separation of the duplicated ureters can lead to injury of the longitudinal blood supply running between the 2 ureters.

What are the important surgical principles when correcting VUR?

1. Adeqate mobilization of the distal ureter without tension or injury to longitudinal blood supply
2. Creation of a generous submucosal tunnel approximately 5 times the width of the ureter in length as recommended by Paquin (1959)
3. Appropriate manipulation of the ureter and correct positioning in the submucosal tunnel to prevent obstruction, stricture, or persistent VUR following surgery
4. Careful bladder handling to prevent significant postoperative hematuria and bladder spasms

Both intravesical and extravesical approaches are used to correct VUR. What unique and significant complication is seen only in extravesical repairs?

1. Transient urinary retention seen in up to 20% of patients following bilateral extravesical repairs
2. Thought to be due to the use of excessive electrocautery during ureteral mobilization with subsequent injury to the pelvic plexus nerves situated approximately 2 cm distal and medial to the UVJ

Surgery goes well.

What is your post-surgical follow-up?

1. Continue prophylactic antibiotics for several months following surgery
2. RBUS 1–2 months after surgery to rule out ureteral obstruction
3. A postoperative VCUG is not required if the child is doing well clinically as the success rate of the operation is ~96% in children with 1–4 grades of VUR. Those with grade 5 VUR and duplicated collecting systems have lower success rates and may require a postoperative study

What are your recommendations for follow-up?

1. Annual height, weight, BP and urinalysis for protein and infection through adolescence
2. Counsel parents and child of the need for good bladder and bowel habits

Change the scenario to a 5-year-old girl with continuous incontinence. Her parents state that she has never been dry. She voids regularly but has continuous leakage with signs of perineal irritation and damp underwear.

What is your differential diagnosis?

1. Bladder-bowel dysfunction with urinary incontinence
2. Neurogenic bladder
3. Ectopic ureter

What is the next step in evaluating a girl with continuous incontinence and suspicions that she may have an ectopic ureter?

1. Confirmatory diagnosis can be elusive
2. RBUS is typically normal. Subtle clues on RUS are findings suspicious for a renal duplication. Occasionally upper pole hydroureteronephrosis is found
3. An exam under anesthesia with cystovaginoscopy can be helpful. Injection of methylene blue or indigo carmine may aid in the diagnosis
4. The best imaging study is a MR urogram with delayed images looking for an upper pole cap with a dilated ureter seen down to the level of the bladder. At times a dilated ureter can be seen going into the vagina with fluid (urine) seen in the vagina

What are the treatment options when an ectopic ureter causes continuous incontinence?

1. Ipsilateral upper to lower ureteroureterostomy
    a. Either in the lower ureter or proximal ureter near the renal pelvis. More commonly this is done at the level of the lower ureter to hide the scar using a small inguinal incision or with the laparoscopic robotic-assisted approach
2. Common sheath ureteral reimplantation
3. Upper pole heminephrectomy and subtotal ureterectomy

Why do girls with ectopic ureters present with urinary incontinence but boys do not?

1. The common nephric duct when absorbed in males is never associated with structures below the pelvic floor and sphincter
2. In females, abnormal embryologic events can lead to an ectopic ureter draining into the vagina, uterus, and distal urethra, hence the continuous incontinence

CASE 7

HPI: A newborn infant presents with an abdominal mass. Screening prenatal ultrasound at 20 weeks was normal. Normal amniotic fluid was present. Pregnancy and delivery were uneventful; infant born at term. Apgar scores 9 and 9. Normal respiratory status. Infant has voided. Maternal history unremarkable; no drug use. No urologic problems in the family. No other children in the family.

PMH: none

PSH: none

Allergies: none **Medications:** none

FH: mother with history of VUR, status post ureteral re-implantation
SH: lives with mother
ROS: unremarkable

PE:

Vitals	T 98.6 BP 84/52 P 174 RR 30
GA	no distress; well-developed, well-nourished newborn F
HEENT	EOMI, PERRLA
Heart	RRR
Lungs	CTA B
Abdomen	soft; non-distended; RUQ firm mass
Back	(-) dimple; (-) hairy patch
GU	normal female genitalia
Anus	normal position
Neuro	normal
Ext	normal pulses; normal tone

What initial lab tests do you order?

UA/microscopy→ negative
BMP → normal electrolytes; creatinine 0.9 mg/dL

What is a normal serum creatinine in a newborn?

0.2–0.4 mg/dL.

How do you explain the creatinine of 0.9 mg/dL?

Reflection of mother's serum creatinine.

Repeat creatinine in 2–3 days is 0.4 mg/dL.

Besides labs, what else is indicated in the initial workup of this newborn with abdominal mass?

RBUS:

1. Right kidney with multiple cysts, the largest is in the periphery. The cysts do not appear to communicate and the central sinus echo is absent
2. Left kidney with mild hydronephrosis
3. No ureteral dilation
4. Bladder appears normal

What is your differential diagnosis for the right kidney?

1. Multicystic dysplastic kidney
2. UPJ obstruction
3. Vesicoureteral reflux

What additional imaging would you want at this point? Any additional interventions?

1. VCUG and nuclear renogram
2. Prophylactic antibiotics should be started (Amoxicillin or Keflex)

IMPORTANT: do NOT give child under 2 months of age Bactrim/Septra (risk of kernicterus) or Nitrofurantoin (risk of hemolytic anemia).

Results:

1. VCUG
    a. Normal bladder and urethra; left grade 3 VUR; no VUR on right
2. Nuclear renogram
    a. Discuss differences between MAG-3, DTPA, and DMSA
        i. MAG-3: secreted in proximal tubule
        ii. DTPA: filtered by glomerulus, measures GFR (should not be used in patients with renal insufficiency). Less anatomic detail. Not typical agent used in children
        iii. DMSA: assess cortical scarring and function
        iv. Results of NM scan show nonfunctioning right kidney; normal function on the left

What is the assessment at this point?

Newborn female with right multicystic dysplastic kidney and left vesicoureteral reflux.

What do you recommend for this child? Discuss each kidney separately.

1. Observation of the right MCDK
2. Continue antibiotic prophylaxis for the left VUR. Amoxicillin or Keflex until 2–3 months of age, then switch to Bactrim or Nitrofurantoin

What are the indications for operating on MCDK?

Respiratory distress and difficulty with feeding due to mass effect.

What are the general recommendations for managing a child UNDER 1 year of age with VUR?

Continuous antibiotic prophylaxis (CAP) is recommended if child has grade III-V VUR or has had a febrile UTI.

What are the general recommendations for managing a child OVER 1 year of age with VUR?

1. Evaluate for bladder/bowel dysfunction (BBD), and if present, the child should be on CAP
2. CAP is an option if BBD absent and there is a history of UTI

What is the recommended protocol for follow-up in children with VUR according to the AUA guidelines?

1. Annual BP, height, weight, urinalysis, and periodic RBUS
2. VCUG between 12 and 24 months
3. Nuclear renogram (DMSA) if RBUS abnormal, elevated creatinine, or new concern for scarring

5 years later the child returns to the ER with fever, chills, nausea and vomiting. The family had stopped coming for clinic visits after 2 years. However, the child has remained on CAP. No recent imaging has been done. On exam she is febrile and tachycardic with left flank pain.

What initial lab tests would you order?

UA/microscopy → 75–100 WBC/hpf and many bacteria
Urine Cx → >100,000 colonies Enterococcus (pansensitive)
BCx → negative
BMP → creatinine 0.4 mg/dL

What is your next step in management?

Admit, resuscitate with IVFs, and start broad spectrum antibiotics.

Over 24 hours the child becomes afebrile and clinically improves.

What is your next step?

IMPORTANT: Make sure she is on appropriate antibiotics at the time the VCUG is performed.

RBUS: left kidney 9 cm in longitudinal length (large for age) with mild hydro and cortical thinning of the upper pole; right kidney 1.8 cm (involuted MCDK); bladder normal

DMSA nuclear renogram: decreased uptake in wedge shaped area of left upper pole; non-functioning right kidney

VCUG: Grade III VUR on the left

Now that she has had a breakthrough infection how does your management strategy change?

Surgical intervention for the VUR is indicated

Surgical options include:
1. Endoscopic injection of bulking agent
2. Ureteral re-implantation

What are the absolute indications for surgical intervention?

1. Medical noncompliance with CAP

2. Breakthrough UTI on CAP
3. Progressive scarring
4. Associated UVJ abnormality

What are the goals of intervention?

1. Reduce episodes of pyelonephritis
2. Maximize normal renal growth and prevent future renal scarring
3. Reduce risk of hypertension and renal failure

Parents elect for ureteral re-implantation.

Describe different techniques.

1. Intravesical ureteral re-implant procedures:
   a. The Politano-Leadbetter technique creates a new ureteral hiatus more cephalad to the original ureteral hiatus. A new submucosal tunnel is created in an orthotopic fashion. A long tunnel can be created with this technique
   b. Glenn-Anderson technique uses original hiatus with advancement of ureter distal towards the bladder neck. Kinking of ureter does not occur with this technique. However tunnel length is shorter than other procedures
   c. Cohen repair creates a ureteral tunnel that is directed laterally across the trigone (trans-trigonal) towards the contralateral orifice. Suited best in situations in which the bladder is small, or when posterior bladder wall or bladder neck surgery is also done
2. Extravesical ureteral re-implant procedures:
   a. Lich-Gregoir repair with modifications advances the ureter distally with lengthening of the tunnel made by creation of muscular trough for ureter. Bladder is not open and bladder spasms are less

What is your post-operative management?

1. STANDARD (AUA Guideline) is to perform RBUS, typically 4–6 weeks after surgery to rule out ureteral obstruction
2. Continue CAP for 3–6 months with option of performing postoperative VCUG to confirm resolution of VUR

What are potential complications of reimplantation?

1. Recurrent UTI
2. Contralateral reflux
3. Persistent reflux
4. Kinking of ureter (seen after Politano-Leadbetter technique) related to "J-hooking" when bladder full resulting in intermittent ureteral obstruction
5. UVJ obstruction
6. Bladder diverticulum
7. Urine leak
8. Urinary retention (injury to pelvic nerves with bilateral extravesical method)

What is your long-term follow-up plan after successful surgery?

1. Because the contralateral kidney is abnormal—yearly BP, height, weight, UA, and creatinine through adolescence
2. If contralateral kidney was normal, the above testing is optional

What are the long-term consequences of VUR that parents should be informed about?

1. Hypertension
2. Renal scarring and functional loss
3. Recurrent UTIs
4. Familial VUR in sibling and offspring

Related Information

What is the incidence of VUR in siblings?

27%

When is screening of a sibling indicated? How is that accomplished?

1. Indications: renal cortical abnormality, size asymmetry on RBUS, or history of UTI
2. Test: radionucleotide cystogram or VCUG

Describe the International Reflux Classification of VUR.

Grade I:	Reflux to ureter
Grade II:	Reflux to ureter and collecting system, no dilation
Grade III:	Mild dilation of renal pelvis and calyces
Grade IV:	Moderate dilation of renal pelvis and calyces
Grade V:	Severe dilation of renal pelvis and calyces with ureteral tortuosity

What is historically considered the normal submucosal tunnel to ureteral diameter ratio?

5:1

What are the primary causes of VUR?

1. Short intramural ureter (ratio of submucosal length to diameter <5:1)
2. Absence of adequate detrusor backing
3. Lateral displacement of the ureteral orifice
4. Abnormal configuration of the ureteral orifice

What are the secondary causes of VUR?

1. Neurogenic bladder
2. Bladder outlet obstruction
3. Paraureteral diverticulum
4. Cystitis
5. Detrusor instability
6. Duplicated collecting system (with or without ureterocele)

Which areas of parenchyma are most susceptible to scarring? Why?

Upper and lower poles.

They contain compound papilla with large open collecting ducts, which allow for intrarenal reflux of urine

What is the pathophysiology of acquired renal scarring?

1. Typically occurs secondary to reflux of infected urine
2. Immunologic response to bacteria causes release of oxygen free radicals and proteolytic enzymes, which injures renal parenchyma

CASE 8

HPI: A 3-year-old female presents with a right abdominal mass. Child's grandmother noticed the mass during a bath 2 weeks ago. Child is healthy. Pregnancy and delivery were uneventful. Infant born at term. Child has reached normal developmental milestones. No history of gross hematuria, UTI or trauma. Immunization are up to date.

PMH: none

PSH: none

Allergies: none **Medications:** none

FH: mother with history of recurrent UTIs
SH: lives with parents and older brother
ROS: mother described increased lethargy

PE:

Vitals	T 98.6	BP 140/90	P 100	RR 14
GA	no distress; well-developed; well-nourished			
HEENT	EOMI; PERRLA			
Heart	RRR			
Lungs	CTAB			
Abdomen	firm; smooth; non-tender mass palpable in RUQ			
Back	no dimples or hairy patch			
GU	normal female genitalia			
Anus	normal position and tone			
Ext	normal pulses; normal tone			
Neuro	normal			

What initial lab tests do you order?

UA/microscopy → 20 RBCs/hpf; 0–1 WBCs/hpf: no bacteria
BMP → Creatinine 0.5 mg/dL

What imaging studies would you order?

RBUS: demonstrates a 12 cm heterogenous mass occupying almost entire right kidney. The left kidney and bladder are normal

What is your differential diagnosis? Which is most likely?

1. Wilms' tumor
2. Congenital mesoblastic nephroma (most common renal tumor in infants)
3. Neuroblastoma (not a renal mass but can present as an abdominal mass)
4. Clear cell sarcoma
5. Rhaboid tumor
6. Renal cell carcinoma
7. Angiomyolipoma

What is the next step?

CT scan of abdomen of pelvis.

CT scan confirms solid right 12 cm heterogeneous mass.

What other studies would you order?

1. CBC with platelets and comprehensive melabotic profile (CMP)
2. If concerns for intracaval tumor extension, MRI (if ultrasound cannot exclude tumor extension)
3. Chest CT
4. Cranial CT or cranial MRI if pathology confirms clear cell sarcoma or rhabdoid tumor
5. Skeletal survey or bone scan if pathology confirms clear cell sarcoma or renal cell carcinoma

What congenital anomalies are associated with Wilms' tumor?

1. WT1 gene: 11p13—Non-overgrowth syndromes
    a. WAGR Syndrome
        i. Wilms' tumor, Aniridia, genital anomalies, mental retardation
        ii. 30% risk of Wilms' tumor
    b. Denys-Drash
        i. Male pseudohermaphroditism, renal mesangial sclerosis, Wilms' tumor
        ii. 90% risk of Wilms' tumor
2. WT2 gene: 11p15—Overgrowth syndromes
    a. Beckwith-Wiedemans syndrome
        i. Hemihypertrophy, Macroglossia, Visceromegaly, Omphalocele
        ii. 5% ris
    b. Hemihypertrophy
    c. Perlman syndrome—visceromegaly, macrosomia, polyhydramnios, adnormal facies
    d. Sotos syndrome—macrocephaly, developmental delay

What are some clinical features/presentation of Wilms' tumor?

1. Most children are otherwise healthy, present with only mild constitutional symptoms
2. Palpable mass (90%)
3. Hematuri (25%)
4. HTN (25%)
5. Girls = Boys
6. Median age 3.5

What are the most common sites of metastasis?

1. Lung
2. Regional lymph nodes
3. Liver

Can you define her stage at this point?

No, staging is surgical.

What are the treatment options?

Surgery—Right radical nephrectomy.

Describe the surgical technique.

1. Transperitoneal approach
2. Inspect and palpate all 4 quadrants for local extension, liver, nodal, and peritoneal seeding
3. Inspecting contralateral kidney *no longer recommended* if adequate MRI or CT done pre-op
4. Palpate IVC and renal vein for thrombus
5. Complete the nephrectomy, without tumor spillage
6. Sample suspicious nodes—formal retroperitoneal lymph node dissection is not necessary

What if you are unable to resect the mass?

Treatment using chemotherapy typically makes nephrectomy possible.

In what other clinical situation is preoperative chemotherapy recommended?

Bilateral Wilms' tumors.

Pathology returns—Favorable histology

Describe favorable histology?

1. Intrarenal pseudocapsule—compressing adjacent normal parenchyma
2. "Classic" triphasic components—blastemal, epithelial, and stromal components

Describe unfavorable histology?

Anaplasia: nuclear enlargement, hyperchromasia, abnormal mitotic figures.

1. Associated with resistance to chemotherapy
2. Poor prognosis even when confined to the kidney (stage I)

What is the staging of Wilm's tumor?

Stage I	Confined to kidney, completely resected, no intra-op spillage
Stage II	Extracapsular penetration, completely resected, may have renal sinus extension or vessel invasion
Stage III	Residual tumor in abdomen (nodes, spillage, peritoneal implants, incomplete resection)
Stage IV	Hematogenous metastases to the lung/liver/bone/brain
Stage V	Bilateral at diagnosis

What are the risk factors for recurrence?

1. Tumor spillage
2. Unfavorable histology
3. Incomplete excision
4. Failure to sample lymph nodes resulting in under staging

What is the mainstay of treatment after surgery?

Chemotherapy and radiation based on stage.

After radical nephrectomy, what is the therapy according to stage?

Vincristine (VCR)
Dactinomycin (AMD)
Doxorubicin (DOX)
Cyclophosphamide (CPM)
Etoposide (VP-16)
Radiation (XRT)

1. Favorable histology:
   a. Stage I & II   VCR + AMD
   b. Stage III & IV   VCR + AMD + DOX + XRT
2. Unfavorable histology (Anaplastic):
   a. Stage I   VCR + AMD + DOX + XRT
   b. Stage II–IV   VCR + AMD + DOX + CPM + VP-16 + XRT

What is an important principle in the treatment of stage V (bilateral) disease?

1. Neoadjuvant chemotherapy
2. Surgical therapy of each kidney is handled individually
   a. Nephrectomy, partial nephrectomy, wedge resection, enucleation
   b. Address less affected side first

What are the indications for neoadjuvant chemotherapy?

1. Bilateral tumors
2. Tumors too large to excise safely
3. IVC involvement above hepatic veins

What are the major side effects of chemotherapy?

1. Dactinomycin—myelosuppression
2. Vincristine—neurotoxicity
3. Doxorubicin—cardiotoxicity
4. Etoposide—myelosuppression

What are the major side effects of radiation therapy?

1. Scoliosis, if vertebral column adjacent to the renal fossa is irradiated
2. Radiation pneumonitis
3. Nephritis
4. Hepatitis

What patients should be screened for Wilms' tumor?

1. Aniridia
2. Hemihypertrophy
3. Beckwith-Wiedemann (4–7% risk)
4. Denys-Drash (recommend bilateral nephrectomy prior to renal transplantation)

How?

Renal ultrasound every 3 months until age 7.

Other related tumors:

1. Clear Cell Sarcoma
   a. 3–5% childhood renal tumors
   b. No associated syndromes
   c. Unicentric, unilateral
   d. Associated with brain and bony metastases
2. Rhabdoid Tumor
   a. 2% childhood renal tumors, median age <16 months
   b. Hypercalcemia, brain metastases common
   c. Typically poor prognosis
3. Congenital Mesoblastic Nephroma
   a. Most common renal tumor in infants
   b. 3 subtypes: classic, cellular, and mixed
   c. Treatment: radical nephrectomy and adjuvant chemotherapy for cellular type or incomplete resection

CASE 9

HPI: 28-year-old, G2P1 female pregnant with a 32-week-old male fetus with bilateral hydronephrosis and bladder wall thickening. Referred to you by the maternal-fetal medicine service (MFM) for possible prenatal intervention and postnatal management. The patient had a screening obstetrical ultrasound at 20 weeks, which demonstrated mild bilateral hydronephrosis. Serial prenatal ultrasounds have demonstrated progressive hydronephrosis. The fetus is otherwise normal. No evidence of oligohydramnios.

What is your differential diagnosis?

1. Posterior urethral valves
2. Prune belly syndrome
3. VUR
4. Neurogenic bladder
5. Urethral atresia

What is the next best step?

1. Observation with continued management by MFM
2. Discuss with MFM regarding timing of delivery
3. Consider checking a fetal amniotic fluid lecithin-sphingomyelin ratio. This is a test of fetal lung maturity. Lecithin release increases with lung development, while sphingomyelin is generally static. A lecithin-sphingomyelin ratio of >2 indicates fetal lung maturity and a lower risk of postnatal pulmonary issues

What are the indications for prenatal intervention with placement of a vesicoamniotic shunt?

Sonographic urinary tract obstruction with:

1. Sonographic confirmation of singleton pregnancy without other major organ system anomalies
2. Oligohydramnios or anhydramnios
3. Chorionic villus sampling or amniocentesis documenting a male karyotype and absence of chromosomal anomalies
4. Fetal age of less than 25 weeks
5. Favorable fetal urine values based on 2–3 separate aspiration procedures over 5–7 days:
    a. Sodium <100 mEq/L
    b. Calcium <8 mg/dL
    c. Osmolarity <210 mOsm/L
    d. β-2 microglobulin < 4 mg/dL
    e. Protein <20 mg/dL

The patient delivers a baby boy born at 38 weeks who is admitted to the NICU for respiratory distress. You are called to the NICU to evaluate him.

Further history obtained:

Maternal history unremarkable. Delivery was unremarkable. No urologic problems in family. Normal amniotic fluid seen. Apgar scores 6 and 7. Infant has not voided since birth. Infant with labored, tachypneic breathing.

PMH: healthy; previous uneventful pregnancy with vaginal delivery of 2-year-old son

PSH: none

Allergies: none **Medications:** prenatal vitamins

FH: no urological history
SH: lives with husband and son
ROS: unremarkable

PE:

Vitals	T 99.6	BP 92/54	P 180	RR 50
GA	mild respiratory distress; on 4L nasal cannula O2			
HEENT	nasal flaring			
Heart	sinus tachycardia			
Lungs	crackles throughout; poor air movement in lung bases.			
Abdomen	distended; bladder palpable to level of his umbilicus			
Back	(-) dimple; (-) hairy patch			
GU	normal external male genitalia			
Anus	normal anatomic position			
Ext	normal pulses; normal tone			
Neuro	no deficits			

What is your next step?

Placement of indwelling catheter or feeding tube.

You are unable to place the catheter.

What do you next?

1. Can temporize by draining bladder by performing suprapubic aspiration
2. Consider vesicostomy in the OR or in unstable patient at the bedside in the NICU with anesthesia support

What are the important technical points when creating a Blocksom cutaneous vesicostomy?

1. Adequately mobilize the dome of the bladder and resect urachal remnant
2. Secure the bladder at the level of the fascia
3. Create a capacious stoma through the skin and fascial defect of at least 22 Fr in size

You are able to place an 8 Fr Foley catheter in his bladder with good return of urine output. The NICU service places the boy on broad spectrum antibiotics.

What is your next step?

You order a renal bladder ultrasound.

The ultrasound demonstrates severe bilateral hydroureteronephrosis, a thickened bladder wall, and ascites.

What is your next step?

Keep catheter in place and make sure bladder is drained.

What is the most likely etiology for the ascites?

1. Urinary, from high intraluminal pressures in the urinary tract, which leads to urine extravasation typically across a renal fornix
2. If the ascites is significant and a clinical concern, a paracentesis is indicated
3. Good bladder drainage allows for the site of extravasation to heal

The newborn's serum creatinine on day of life 0 is 1.2 mg/dL. What is the significance of this value?

This value is reflective of the maternal serum creatinine, and generally it takes 5–7 days for the serum creatinine to be a reliable measure of the newborn's renal function.

The newborn is stable several days after delivery and a VCUG is performed.

What radiographic findings are seen in boys with posterior urethral valves?

1. Dilated posterior urethra superior to valve cusps seen during voiding images
2. Thickened and trabeculated bladder
3. VUR, often severe, in around 50% of patients. In those boys with VUR, half will have bilateral VUR
4. Bladder diverticuli

What are the different types of valves as characterized by Dr. Hugh Hampton Young?

1. Type 1 accounts for 95% of cases and begin as leaflets at the distal aspect of the verumontanum and fan out to fuse in the midline just proximal to the external sphincter
2. Type 2 valves in Dr. Young's original classification have been found to be non-obstructing tissue secondary to distal urethral obstruction and are no longer referred to as valves
3. Type 3 valves make up the remaining 5% of the cases and appear as a membrane distal to the verumontanum lying transversely across the urethra with a small perforation near its center. This membrane often appears as a windsock reaching the bulbous urethra with voiding

What other radiographic study would you obtain prior to surgery?

Nuclear renogram using the MAG-3 isotope. This study provides renal differential function and drainage information.

How would you perform the valve ablation?

Cystoscopically using a bugbee electrode, resectoscope with a hook or cold knife, or holmium laser to incise the valve tissue at 5, 7, and as needed at the 12 o'clock positions.

What do you do if you cannot safely ablate the child's valve tissues endoscopically?

Create a cutaneous vesicostomy.

After valve ablation, the boy's creatinine decreases to 0.4 mg/dL over a period of a week. His respiratory status and abdominal distension resolve. However on repeat ultrasound several weeks following the procedure, he continues to have persistent hydroureteronephrosis.

What is your next step?

1. Observation. Persistent hydroureteronephrosis is common following successful surgery and the vast majority of boys do not have obstruction at the UVJ or bladder outlet
2. In a minority of boys, the degree of hydroureteronephrosis warrants repeat nuclear renography, or more rarely, a Whitaker test to assess the UVJ

The child does well after his valve ablation and sees you routinely in clinic without any significant urologic issues. Unfortunately, he begins to have issues with recurrent UTIs at 3 years of age and is having issues with toilet training. His RUS demonstrates bilateral mild hydroureteronephrosis.

What is your next step?

1. Repeat VCUG to rule out persistent valve tissue and VUR
2. If VCUG demonstrates no valve tissue, then perform urodynamics to assess bladder storage and emptying
3. If he has VUR and normal bladder dynamics, consider anti-reflux surgery if child has continued UTIs on prophylactic antibiotics
4. If no VUR but abnormal urodynamics, treat appropriately based on urodynamics. Younger boys in general have issues with detrusor hyperreflexia and decreased bladder size and compliance. Older boys have myogenic failure. Patients may require anti-cholingerics, α-blockers, intermittent catheterization, continuous nocturnal bladder drainage, timed voiding, or any combination of these measures
5. A small percentage of boys will require augmentation cystoplasty and creation of a continent catheterizable channel to lower intravesical pressures and help with bladder emptying

What is the valve bladder syndrome?

1. A constellation of findings, described by Dr. Mike Mitchell, in which valve patients have intrinsic bladder dysfunction leading to deterioration of the upper tracts and urinary incontinence despite successful valve ablation
2. Boys typically have poor bladder sensation, which leads to high bladder volumes and poor compliance . Over time, this has a deleterious effect on the upper tracts and can lead to urinary incontinence

CHAPTER 15

RENAL TRANSPLANTATION

MOHIT GUPTA, MD
LAWRENCE YEUNG, MD

CASE 1

HPI: 41-year-old African-American male has been referred to your clinic for evaluation for a living donor nephrectomy to his 45-year-old brother with end-stage renal disease secondary to polycystic kidney disease. The patient is otherwise healthy and underwent a prior CT scan at age 35 to evaluate for polycystic kidney disease; the CT was unremarkable.

PMH: none

PSH: none

Allergies: none **Medications:** none

FH: (+) IDDM; (+) polycystic kidneys in older brother
SH: (-) tob; (-) ETOH
ROS: non-contributory

PE:

Vitals	T 98.6	BP 120/60	P 80	RR 14
General Exam	well-developed, well-groomed adult AAM			
HEENT	benign			
Heart	RRR			
Lungs	breathing comfortably on room air			
Abdomen	soft; non-tender; non-distended; no surgical incisions			
Flank	(-) CVAT			
GU	normal male			
Prostate	benign			
Ext	(-) CCE			
Neuro	non-focal			

What laboratory and diagnostic testing would you obtain?

State that you would obtain ABO and HLA typing with crossmatch, CBC, CMP including fasting plasma glucose, coagulation studies, viral serologies (Hep B, C, HIV), urinalysis with culture (if indicated), and 24-hour urine collection for protein and creatinine or spot albumin:creatinine ratio for assessment of GFR.

A chest x-ray and EKG should also be performed, with further testing dependent on risk profiles and recommended health maintenance guidelines (i.e., CT chest, PFTs in smokers, mammogram in females age >40, colonoscopy in patients age >50, PSA in Caucasian men age >50 or African-American men age >40), stress testing if EKG abnormal or significant cardiac history).

CBC, CMP, LFTs → normal
Lipid Panel, Fasting glucose → normal
Urinalysis → normal
UCx → no growth
Creatinine clearance → GFR >80mL/min/1.73m^2
CT with IV contrast → (L) kidney 2 renal arteries; (R) kidney single A.
PSA → 0.8 ng/mL

HepB Surface Ag, AntiHBc → negative
Anti-HIV or HIV Ab/Ag combo → negative
Anti-HCV → negative
RPR/VDRL → negative
HSV, VZV, EBV, CMV → negative
24-hr Urine Stone panel → Indicated only if hx of >3 mm stone
Hemoglobin A1C → <5%, indicated only if first degree relative +DM
EKG, CXR → normal

What is the importance of the psychosocial evaluation?

Psychosocial evaluation is mandated prior to donation and must be performed by an appropriately credentialed professional. This evaluation focuses on social support, motivation for donation, exclusion of coercion or financial gain, evidence of high-risk behaviors, and designation of a third-party donor-advocate.

What is the accepted age range for renal transplant donors?

There is no clear-cut age limit for kidney donors. The general health of the donor and the age of the recipient are important in this decision and should be reviewed case-by-case. A healthy 75-year-old can give his 74-year-old wife a kidney, but a 20-year-old should not receive that same kidney.

What other considerations must be reviewed prior to kidney donation that could serve as relative contraindications?

1. ABO or HLA incompatibility
2. Planned protocol and informed consent must be obtained
3. Proteinuria and/or hematuria
4. Impaired renal function
5. Defined as GFR <80 mL/min/1.73m2
6. Anatomic abnormalities
7. Marked urologic, renal vascular abnormalities, or multiple renal vessels (e.g., >2 vessels, depending on surgeon experience)
8. Active viral infection
9. HTLV, HBV, HCV
10. Malignancy
11. Lung, breast, renal/GU, GI, hematologic organs, and melanoma
12. Chronic illnesses
13. Pulmonary, liver, autoimmune, neurologic, or cardiac disease
14. Hypertension
15. Nephrocalcinosis, bilateral stones, or recurrent nephrolithiasis
16. Current pregnancy
17. Disorders requiring anticoagulation
18. Atrial fibrillation/Cardiac arrhythmias
19. Venous thrombosis
20. Active peptic ulcer disease
21. History of sickle cell trait
22. BMI >35
23. Familial history
24. Strong history of DM
25. History of RCC

26. Active illicit substance or alcohol abuse
27. Ambivalence to donation

What are 2 major histocompatibility systems of importance in renal transplantation?

1. ABO blood group
2. HLA systems

The donor and the recipient must usually be ABO compatible (but not identical). In experimental protocols, ABO barriers can be crossed with renal transplantation.

What are major histocompatibility antigens?

Human leukocyte antigens. HLAs are glycoproteins located on the cell membrane. These antigens are encoded by major histocompatibility complex (MHC) found on short arm of chromosome 6. Three loci (HLA-A, HLA-B, and HLA-DR) are tested. Since 2 alleles are present, there are 6 possible matches. The more mismatched the recipient, the higher the risk for rejections.

Discuss HLAs and their classification:

The HLAs, also known as MHC, represent a set of highly polymorphic cell surface antigens. They are encoded by a closely linked cluster of genes on chromosome 6. The immune system's discrimination of self and non-self is based on HLA.

1. HLA class I: expressed on all nucleated cells
   a. HLA-A and HLA-B are class I antigens (as well as HLA-C)
   b. Present endogenous antigens to cytotoxic T-cells
2. HLA class II: expressed on cells of the immune system
   a. HLA-DR is a class II antigen (along with HLA-DQ and HLA-DP)
   b. Present antigen to helper-T-cells

What are absolute contraindications for a renal transplant in a recipient?

1. Active malignancy
2. Active infection
3. Active substance abuse
4. Reversible renal failure
5. Documented treatment non-adherence
6. Significantly shortened life expectancy

There is no universally accepted life expectancy that precludes transplantation although many centers are hesitant to transplant patients with life expectancy of <5 years, which is considered the expected half-life of the allograft.

When are cancer patients eligible to receive a transplant kidney?

Immunosuppressant medications may unfavorably influence the natural history of a known malignancy. Recommended tumor-free waiting periods are as follows:

Organ with Malignancy	Recommended Waiting Period
Kidney • Incidental • Large, infiltrating lesion • Wilms' tumor	 • No waiting period • At least 2 years • At least 2 years
Bladder • Carcinoma-in-situ or papillary superficial lesions • Invasive disease	 • No waiting period • At least 2 years
Testis	• At least 2 years
Prostate	• At least 2 years
Breast/Melanoma/Cervix/Colon	• At least 5 years

*Note that eligibility/waiting times may differ from institution to institution.

What are the indications for pre-transplant native nephrectomy?

Native nephrectomy is recommended for those recipients with chronic or recurrent acute bacterial pyelonephritis, infected stones, heavy proteinuria, intractable hypertension, polycystic kidney disease with markedly enlarged kidneys, infected reflux, and concern for renal cystic disease with suspicion of adenocarcinoma.

When is native nephrectomy performed?

Native nephrectomy is performed 6 weeks before transplant.

What is the significance of the small bladder capacity for transplant recipients?

Bladders identified with significant fibrosis and poor compliance may need pre-transplant augmentation. Transplant is possible with similar outcomes in patients with urinary diversion or augments compared to a normal-capacity, native bladder. Even very small bladders may develop normal capacity and compliance post-transplantation unless extensive fibrosis is present.

What do you do now?

Obtain informed consent from the donor, check preoperative labs, and order pneumatic compressive devices, as well as any indicated immunosuppression.

Describe your surgical technique for the Donor Nephrectomy.

The Operation (Hand-assisted Laparoscopic Donor Nephrectomy)

1. Place NGT and Foley catheter
2. Place patient in lateral position (donation side up)
3. Place camera trocar, then additional trocars under direct visualization
4. Introduce handport through a lower midline or lower transverse incision

5. In case of left nephrectomy (most common—due to longer renal vein): mobilize descending colon, dissect ureter, open Gerota's fascia, dissect renal artery and vein, ligate adrenal vein and gonadal vein
6. In case of right nephrectomy: mobilize ascending colon, dissect ureter, open Gerota's fascia, dissect renal artery and vein
7. Clip and cut ureter, clip and cut artery, staple and cut vein
8. Remove kidney via handport and flush with cold conservation liquid via artery (University of Wisconsin or Euro-Collins)
9. Check for bleeding, especially from vascular dissection
10. Close the incisions
11. Transfer to PACU and the floor

Principles of donor nephrectomy:

1. The better kidney stays with the donor: always transplant the kidney with minor anomaly
2. Consider right donor nephrectomy in female of childbearing age (right-sided hydronephrosis of pregnancy)
3. Can be performed open or laparoscopically

How do you manage 2 renal arteries?

State that you would perform side-to-side anastomosis of 2 renal arteries to create "pair of pants."

You successfully create "pair of pants" at the back table and hand the kidney off to the transplant team. You are now informed that the transplant surgeon is unavailable and you are asked to perform the renal transplant.

Principles:

1. Always attempt to preserve lower pole arteries as they often supply blood to the ureter. It is acceptable to tie off small upper pole arteries
2. Small venous branches can be ligated without consequence
3. In cadaveric donors, a short right renal vein can be elongated with the use of the supplied inferior vena cava (almost routinely done for right cadaveric transplant)
4. Cadaveric iliac vessels can be used as extenders for both vein or artery

During the ureteroneocystostomy, you discover the ureter is too short and the distal end appears dusky and ischemic.

What are your options?

For short or ischemic allograft ureters, options include performing a Psoas hitch, Boari flap, native ureteroureterostomy, native ureteropyelostomy, pyelovesicostomy, or ileal ureter to close ureteral gaps.

You performed ureteroureterostomy to the native ureter.

Both the donor and the recipient did well from their surgery and were transferred to the floor.

Discuss surgical complications and treatment.

1. Complications with collecting system and ureter
2. The most common complication is obstruction of the Foley catheter (e.g., due to blood clots)
3. Urine leak at anastomosis is most commonly caused by ureteric ischemia
4. Treatment includes ureteroneocystostomy, ureteroureterostomy to native ureter and pyelovesicostomy
5. Ureteral stricture is caused by ureteric ischemia
   a. Treatment includes percutaneous nephrostomy tube and balloon dilation or ureteral reimplant
6. Calyceal-cutaneous fistula is rare, but potentially life-threatening due to the high risk of sepsis, and is caused by localized area of poor perfusion in the renal parenchyma
7. May be seen in cases of multiple renal arteries and inadvertent ligation
8. Initial treatment includes prolonged percutaneous nephrostomy tube and ante grade stent drainage
9. Surgical exploration with transplant partial nephrectomy, or possibly total nephrectomy, may be required

   Note: Urologic complications are the most common complications of renal transplant surgery.

10. Vascular complications
11. Renal artery stenosis
12. Suspected by graft dysfunction and diagnosed by Doppler ultrasound and/or MR-angiogram
13. Soon after transplantation, reoperation is mandatory
14. Late and sub-acute cases can be treated by angioplasty
15. Renal artery thrombosis
    a. This is a surgical emergency and is suspected by graft dysfunction, diagnosed by Doppler ultra-sound and/or MR-angiogram
    b. Treated by exploration and attempted revascularization
    c. Often nephrectomy must be performed because kidney is not salvageable
16. Renal vein thrombosis
    a. This is a surgical emergency is and suspected by graft dysfunction, diagnosed by Doppler ultrasound and/or MR-angiogram
    b. Treated by thrombectomy and heparinization
    c. If kidney is not salvageable, proceed with allograft nephrectomy
    d. If graft rupture occurs as a result of renal vein thrombosis, perform immediate nephrectomy
    e. Salvage of transplant kidney is rare with thrombectomy and repair of graft rupture
17. Iliac vein thrombosis
18. Diagnosed by color Doppler studies
19. Treated by IV heparinization
20. Arterial or venous anastomotic leak
21. Acute hemorrhage usually occurs within 24 hours
    a. This is treated with an attempt at repair, but nephrectomy may be inevitable
22. Lymphatic complications
23. Lymphocele
    a. Caused by unclipped lymphatics
    b. Large lymphoceles may cause ureteric or venous obstruction
    c. Diagnosed by pelvic US and/or MRI

   d. Treated by creating an intraperitoneal window laparoscopically; open exploration is rarely necessary

Name and define different types of rejection:

1. Hyperacute rejection: occurs immediately after revascularization due to preformed antibodies
   a. Allograft nephrectomy is required
2. Acute rejection: occurs in weeks to months
   a. Currently, acute rejection is typically diagnosed before the patient has any symptoms
   b. Acute rejection is suspected due to declining urine production and elevation of serum creatinine
   c. Diagnosis is confirmed by renal biopsy
   d. Rejections can be predominantly cellular or antibody-mediated and are classified according to the Banff system
3. Chronic rejection and chronic allograft nephropathy (CAN): occurs after years
   a. Gradual decline in renal function
   b. No clear evidence of rejection episode
   c. Diagnosis made by biopsy: minimal mononuclear cell infiltration; interstitial fibrosis and vascular changes

What is the cancer risk with immunosuppression?

Chronic immunosuppressive treatment increases the risk of malignancy. Modulating factors include concomitant viral infections, pre-transplant hemodialysis, sun exposure, as well as the type, degree and duration of immunosuppression.

1. Skin cancer
   a. Squamous cell carcinoma (most common)
   b. Basal cell cancer
   c. Melanoma
2. PTLD/non-Hodgkin lymphoma
   a. Increased risk after induction therapy with T-cell depleting antibodies
   b. Mostly due to Epstein-Barr virus induced proliferation of B-cells
3. Kaposi's sarcoma
4. Carcinoma of the uterine cervix
5. Anogenital cancers
6. Renal cancer

What is the most common infection after renal transplantation?

Immunosuppressive therapy is associated with an increased incidence of infectious complications. The risk correlates with the overall degree of immunosuppression as well as pre-disposing factors (such as indwelling catheters, diabetes mellitus, peritoneal dialysis, and others).

Early after transplantation, conventional bacterial and fungal infections are the most common (such as wound infections, pneumonia or catheter-related infections). After the first month, more "unusual" or "opportunistic" infectious agents can become clinically apparent, such as CMV, Pneumocystis jiroveci (formerly carinii), Listeria monocytogenes, and Aspergillus fumigatus.

How do you manage life-threatening infections in a renal transplant recipient?

During life-threatening infections, immunosuppression should be stopped. Aggressive work-up should be performed, and empiric broad-spectrum antibiotic and/or antiviral treatment should be initiated.

What is the differential diagnosis of renal dysfunction post-transplant?

Differential diagnoses of renal dysfunction include the following:

1. Deterioration of a functioning graft
   a. Foley obstruction
   b. Vascular (arterial thrombosis, venous thrombosis)
   c. Volume depletion
   d. Acute rejection
   e. Ureteral obstruction or leak
   f. Calcineurin inhibitor toxicity (Cyclosporine, Tacrolimus)
2. Poor initial function
   a. Acute tubular necrosis (especially in marginal grafts or long cold storage)

Note: Transient renal dysfunction requiring dialysis early after transplantation is termed "delayed graft function," the most common etiology being acute tubular necrosis. If a kidney never functions, this is called "primary non-function."

How do you evaluate renal dysfunction post-transplant?

Laboratory and special studies for evaluation:

1. Check Foley
2. Check blood pressure
3. Doppler, MRA
4. Labs, including drug levels
5. Percutaneous graft biopsy

Discuss treatment options for renal dysfunction:

1. Acute rejection
   a. Steroid pulse
   b. Treatment of steroid resistant or vascular rejection: monoclonal or polyclonal antibodies; steroid resistant rejection should be documented before antibody therapy
2. Immunosuppression toxicity
   a. Diagnosis of exclusion
   b. Consult with Transplant/Nephrology to adjust dose and/or transition to alternative regimen

Describe differential characteristics of acute rejection versus immunosuppression toxicity.

These 2 entities are extremely difficult to differentiate on clinical grounds. High trough levels of calcineurin inhibitors can point to toxicity. Renal biopsy can reveal typical signs of drug toxicity (tubular vacuolization) in the absence of signs of rejection.

CASE 2

HPI: 25-year-old Caucasian female with a long history of type 1 diabetes mellitus is 3 days status post an uncomplicated living-related renal transplant and presents with fever to 102.1° and right lower abdominal pain. She denies nausea, vomiting, or hematuria. The patient's urine output has steadily decreased over the last 24 hours. Her native kidneys remain in-situ; her transplant was placed in the right iliac fossa. She is currently on Cyclosporine, Mycophenolic acid (MMF), and Prednisone per the Transplant team.

PMH: (+) type 1 diabetes mellitus

PSH: (+) renal transplant; has native kidneys

Allergies: Codeine

Medications: Cyclosporine; Mycophenolic acid (MMF); Prednisone; Septra

FH: (+) IDDM
SH: (-) tob; (-) ETOH
ROS: non-contributory

PE:

Vitals	T 102.6	BP 120/60	P 100	RR 14
GA	ill-appearing CF			
HEENT	benign			
Heart	RRR			
Lungs	CTA			
Abdomen	soft; moderately tender RLQ; (-) rebound or guarding incision intact; (-) wound discharge; (-) bruits.			
Flank	(-) CVAT			
Ext	(-) CCE			
Neuro	non-focal			

What initial lab tests do you order?

UA → WNL
CBC → WNL
UCx → no growth
Chem 7 → Cr 1.0 mg/dL; rest of the lab WNL
Cyclosporine → normal

What initial imaging studies would you obtain?

Obtain renal transplant ultrasound and KUB.

KUB: normal; (-) stent
Renal US: moderate amount of perinephric fluid collection

What is your differential diagnosis of a perinephric fluid collection and decreased urine output?

Differential diagnoses of fluid collection around the kidney include:

1. Blood → hemorrhage from arterial or venous anastomosis

2. Urine → urinoma
3. Lymph → lymphocele (unlikely to occur this early in her post-op course)

What is your next step?

The fluid should be sampled through percutaneous aspiration and drain placement with fluid analysis for creatinine, Gram staining, and aerobic/anaerobic culture, as well as KOH prep and fungal culture.

The results of the studies are shown below:

Fluid Cr → 32.0 mg/dL
Serum Cr → 1.0 mg/dL
Fluid culture → (-) growth
Gram's stain → (-) bacteria
KOH stain → (-) fungus

What is your assessment?

The fluid creatinine is markedly elevated in comparison to the serum value, suggesting a urine leak. Serum and fluid creatinine would be consistent in a lymphocele or hematoma, and fluid hematocrit would be elevated in a hematoma.

What is your next step?

The location of the leak should be identified through additional imaging studies, as urinary extravasation often requires open surgical repair. Retrograde or CT cystogram will usually document leakage at the ureteroneocystostomy. If extravasation is not apparent on retrograde cystogram, contrast CT is suggestive, with percutaneous antegrade pyelography confirmatory for extravasation from the ureter or renal pelvis.

In this patient, a retrograde cystogram does not readily demonstrate extravasation, so a percutaneous nephrostomy is placed as the next step for antegrade pyelography. This is positive for leak at the anastomotic site. Delayed renal recovery post-op often precludes administration of IV contrast.

What is your immediate management?

Small leaks may be completely managed with bladder decompression, with or without percutaneous nephrostomy placement or ante grade/retrograde stent placement. Since the leak is from the anastomosis, a stent and Foley catheter should be placed. This was performed, and the nephrostomy tube was also left open to gravity drainage.

After 5 days, she has continued urine output from the drain. Urine output from the nephrostomy and Foley catheter is minimal.

What are your treatment options?

Surgical revision of the anastomosis is necessary and is often preferable for early leaks, necrotic ureter, or failure of the above endoscopic management. Discuss the below treatment options and provide a recommendation from the following:

1. Ureteral reimplantation
    a. This is a reasonable protocol; however, if primary anastomosis cannot be performed, be prepared to discuss other surgical options
2. Ureteropyelostomy to native ureter
    a. The native ureter is mobilized to the renal pelvis of the transplanted kidney, with preparation for nephrectomy of the native kidney
3. Ureteroureterostomy to native ureter
    a. The ureter of the transplanted kidney is connected to the native ureter, with nephrectomy of the native kidney
4. Boari flap to renal pelvis
    a. Anastomosis done using Boari flap from the bladder to the renal pelvis of the transplanted kidney
5. Vesicopyelostomy
    a. Anastomosis performed with the renal pelvis of the transplanted kidney to the bladder.
6. Vesicocalycostomy
    a. Anastomosis between renal pelvis and most accessible calyx (typically lower pole)
7. Ileal ureter
    a. Interposition of short segment of ileum between renal pelvis and bladder

The patient underwent open exploration, and ureteral re-implantation was attempted but was unsuccessful. Thus, you resorted to ureteropyelostomy to native ureter (with stent) and removal of the native kidney. She tolerated the procedure well without complications.

The stent was removed at a clinic follow-up visit 3 weeks later.

If the fluid were to be lymph, what are the treatment options?

Small lymphoceles may be asymptomatic and do not require treatment. The larger a lymphocele, the more likely it is to become symptomatic and require intervention. The presentation of a significant lymphocele requiring treatment may include pain, ureteral obstruction (rising creatinine) and/or iliac vein compression (ipsilateral leg edema, DVT).

1. Percutaneous drainage
2. Sclerosis with fibrin glue
3. Peritoneal window (laparoscopic or open access)

CHAPTER 16

UROLOGIC PROBLEMS OF PREGNANCY

AKIRA YAMAMOTO, MD
LAWRENCE YEUNG, MD

CASE 1

HPI: 28-year-old pregnant female presents with abdominal and (R) flank pain that radiates to the groin for the past 24 hours. She is in her second trimester, and the pregnancy has been uncomplicated thus far. She has never had this pain before. She complains of nausea and vomiting, gross hematuria. No history of kidney stones.

PMH: (-) UTIs; (-) pyelonephritis

PSH: none

Allergies: none **Medications:** vitamins

FH: (-) stones
SH: (-) tob; (-) ETOH
ROS: non-contributory

PE:

Vitals	T 98.6	BP 130/60	P 90	RR 12
GA	WDWN young female in moderate distress			
HEENT	NCAT			
Heart	RRR			
Lungs	CTA			
Abdomen	soft; NT/ND; gravid			
Ext	warm; well perfused			
Neuro	non-focal			

What initial lab tests do you order?

UA → 20 RBC/HPF; 20–30 WBC/HPF, (-) bacteria
UCx → sent to the lab, pending
Chem 7 → WNL
CBC → WBC 12, H/H 14/38, Plt 200

What is your assessment?

28-year-old pregnant F in her second trimester with right flank pain and gross hematuria secondary to nephrolithiasis or pyelonephritis. Non-urologic etiologies include appendicitis, cholecystitis, diverticulitis, and placental disorders.

What do you do now?

Make sure that she is receiving IV fluids and given a dose of IV antibiotics. Provide pain medication. Of note, both pyelonephritis and renal colic may induce premature onset of labor, which may be stopped with pain medication.

What diagnostic imaging would you obtain?

Renal ultrasound: A renal ultrasound should be obtained first as it causes no adverse effects on the fetus.

Note that abdominal ultrasound has poor sensitivity for direct visualization of a ureteral stone. However renal ultrasonography sensitivity is increased if Doppler ultrasonography is used.

The velocity of intrarenal blood flow can be quantified, and from this a resistive index (RI) can be calculated. RI is defined by peak systolic velocity minus the end diastolic velocity, divided by peak systolic velocity: (PSV-EDV)/PSV.

An elevated resistive index > 0.7 has a sensitivity of 70–92% and a specificity of 83–98% for acute urinary obstruction. An inter-renal difference in resistive index of 0.06 and asymmetric absence of ureteric jet additionally supports the diagnosis.

Endovaginal ultrasound may also be utilized to directly visualize distal ureteral stones or visualize ureteral jets.

The renal ultrasound reveals mild bilateral hydronephrosis, right greater than left.

What is your interpretation of the ultrasound results?

The findings can be explained by either physiologic hydronephrosis or ureteral obstruction.

Physiologic hydronephrosis is seen in 80–90% of women by mid-pregnancy. This is caused by a number of mechanisms, including progesterone mediated smooth muscle relaxation, mechanical compression by ovarian veins and the uterus (right greater than left secondary to dextrorotation of the gravid uterus), and increased blood volume, renal perfusion and urine production. Note that ureteral dilation due to physiologic causes is rare below the pelvic brim.

Ureteral obstruction due to stone on the right could explain the right greater than left hydronephrosis.

What other imaging studies could help you make the diagnosis?

1. Renal US
    a. Initial imaging modality of choice in pregnant patient (no radiation exposure)
    b. Diagnosis of ureteral calculus can be unreliable due to poor visualization of ureter, some studies quote < 50% accuracy
    c. Doppler ultrasonography increases sensitivity and specificity by using resistive index and identification of ureteral jets
    d. Consider vaginal US for distal ureteral stones
2. Limited IVP
    a. This has historically been an excellent second line imaging modality; however, many centers no longer perform traditional IVPs and this can be problematic
    b. Typically, a limited IVP consists of a scout, 30 second and 20 minute films
    c. Approximately 0.20–0.25 rad is delivered to the fetus
3. Low Dose CT
    a. Addition of low dose CT scan greatly increases the ability to diagnose an obstructing ureteral stone. Studies have shown a positive predictive value of 95.8% when combined with US
    b. Delivered radiation dose has been reduced dramatically over the past 20 years with computed image processing techniques
    c. Calculated intra-abdominal organ exposure based on cadaver studies is <15 mGy

   d. The urologist should discuss the risk of radiation exposure with the family but should strongly consider low dose CT if it is available at his/her institution
4. Renal nuclear scan
   a. May be helpful in determining obstruction but has limited anatomical detail
   b. Note that radioactive iodine readily crosses the placenta and can affect the fetal thyroid after 10–12 weeks gestation
5. MRI
   a. Attractive since it has no radiation exposure for the fetus
   b. Sensitive for identifying hydronephrosis and the level of obstruction but does not visualize stones well
   c. Both costly and time-consuming

What is the risk of radiation exposure to the fetus?

The American College of Obstetrics and Gynecology guidelines state that all women should be counseled that radiograph exposure from a single diagnostic procedure does not result in harmful fetal effects.

Ionizing radiation can result in 2 potential harmful effects:

1. Cell death and teratogenic effects:
   a. Data from animal studies suggest that exposure to high dose radiation before implantation will result in death of the embryo. The "all or none" phenomenon
   b. Teratogenic effects are seen when animal embryos are exposed to large doses of radiation (100–200 rad)
   c. Human studies are based on survivors from the atomic bomb, which identified the greatest central nervous system effects with exposure between 8–15 weeks gestation
   d. Growth restriction, microcephaly, and mental retardation are the most common effects and occur at doses of at least 20 rad
   e. According to the ACOG and the National Council on Radiation Protection, the fetal risks of anomalies, growth restriction, or abortion are not increased with a radiation exposure of less than 50 mGy or 5 rad
2. Carcinogenesis:
   a. Risk of carcinogenesis to the fetus is unclear but is believed to be very small
   b. According to the ACOG, it is estimated that a 1–2 rad fetal exposure may increase the risk of leukemia by a factor of 1.5–2.0 over natural incidents. This increases the risk from a background rate of about 1 in 3000 to about 1 in 2000

The dose of radiation is measured as the Rad (rad) or Gray (Gy), whereby 1Gy = 100 rad.

You obtain a low dose CT scan which clearly identifies a 7 mm right mid ureteral stone with associated hydroureteronephrosis and perinephric stranding.

What is your next step?

Admit the patient, place her on IVF, antibiotics, and provide pain control.

Treatment options:

1. Observe with medical expulsive therapy

   a. If the patient is hemodynamically stable and there are no signs of worsening infection, she may choose observation. Studies show that there is an 80% chance of spontaneous stone passage of ureteral stones in pregnancy
   b. She should be placed on IV fluids, antibiotics, and pain control. May consider addition of an α-blocker, although make the patient aware that research of α-blockers in pregnancy are limited to small retrospective studies
2. Proceed with ureteral stent, nephrostomy tube placement, or ureteroscopy

After medical expulsive therapy for 48 hours, the patient's pain remains uncontrolled and she has persistent nausea and vomiting.

What is your next step?

Place JJ stent, preferably under US guidance; alternatively use fluoroscopy very sparingly.

Obtain informed consent and make sure to discuss risks of anesthesia and the procedure to pregnancy. Discuss (low) risk of fetal malformation by use of fluoroscopy if necessary.

If unable to place JJ stent, ask interventional radiologist to place a percutaneous nephrostomy tube under ultrasound guidance.

Pregnancy is associated with hypercalciuria that results in rapid stone encrustation. Encourage good hydration and exchange stent or nephrostomy tube at 4–8 week intervals, and then treat the stone after delivery.

What is the role of definitive stone treatment during pregnancy?

Although there is emerging evidence to support a role of primary ureteroscopic stone fragmentation, this generally is NOT a first choice. However, since placement of a stent or nephrostomy tube, especially earlier in pregnancy, has a high rate of encrustation and a need for additional manipulation, the urologist may discuss the risks and benefits of ureteroscopy with the patient.

A systematic review of the safety of ureteroscopy during pregnancy published by Semins in 2009 revealed no significant difference in the rate of ureteral injury or UTI between pregnant and non-pregnant women undergoing ureteroscopy. Johnson published a multiinstitutional retrospective review of 46 ureteroscopic procedures in 45 patients at 5 centers in 2012 which reported only obstetric complications for a rate of 4.3%. Complications included 1 preterm labor at 30 weeks and 1 preterm delivery at 33 weeks.

Shock wave lithotripsy and PCNL should not be offered.

CASE 2

HPI: 33-year-old pregnant Caucasian female presents with fever, abdominal pain, and (R) flank pain. She is 30-weeks pregnant. She is having fever, chills, nausea, and vomiting. (-) Hematuria, vaginal bleeding, or uterine contractions. Her pregnancy has been uncomplicated; however, she was treated for asymptomatic bacteriuria 1 week ago. She complains of frequency, urgency, and dysuria. Most recent prenatal ultrasound was normal. No history of stone disease.

PMH: (+) UTIs; (-) pyelonephritis; (-) stones

PSH: none

Allergies: none **Medications:** vitamins

FH: (-) stones
SH: (-) tob; (-) ETOH
ROS: non-contributory

PE:

Vitals	T 102.6 BP 130/60 P 110 RR 14
GA	WDWN CF in mild distress
HEENT	benign
Heart	RRR
Lungs	CTA
Abdomen	soft; NT/ND; fundal height appropriate for 26-week gestation; fetal monitor normal with fetal HR @150/min
Flank	mild (R) CVAT
Pelvic	normal
Rectal	benign
Ext	(-) CCE
Neuro	non-focal

What initial lab tests do you order?

UA → 10–15 RBC/HPF; 5–7 WBC/HPF; (+) bacteria
UCx → sent to the lab, results are pending
Chem 7 → BUN 10 mg/dL; Cr 0.8 mg/dL
CBC → WBC 16 K/μL

What is your differential diagnosis?

33-year-old pregnant CF with right flank pain and urinary tract infection. Differential includes right pyelonephritis with or without associated nephrolithiasis.

What would you do at this point?

Admit her for parenteral antibiotics, pain control, and IVF.

What are acceptable antibiotics during pregnancy?

Antibiotic	Antibiotic	Notes
Penicillin	Safe	Increasing prevalence of resistance
Cephalosporin	Safe	Good choice of pyelonephritis, especially if there is concern for first line penicillin resistance Ineffective against *Enterococcus*
Clindamycin	Safe	Recommended for the treatment of group B streptococci in penicillin allergic patients
Nitrofurantoin	Safe, but associated with the rare risk of fetal hemolytic anemia in mothers with glucose-6-phosphate dehydrogenase deficiency	Achieves therapeutic levels in urine and is therefore good for lower urinary tract infections and symptomatic bacteriuria but does not achieve adequate tissue penetration and is therefore ineffective in pyelonephritis Inactive against *Proteus* May be used for prophylaxis to prevent recurrent bacteriuria
Aminoglycosides	Safe Theoretical ototoxicity and nephrotoxicity, but none have been reported	Gentamicin is the most commonly used in combination with Ampicillin for the treatment of pyelonephritis
Sulfonamides	1st Trimester: Antifolate teratogenicity 3rd Trimester: hyperbilirubinemia with kernicterus because sulfonamides can displace bilirubin from albumin	
Trimethoprim (TMP)	1st Trimester: TMP inhibits folate metabolism and theoretically could increase the risk of neural tube defects	
Fluoroquinolones	NOT recommended for pregnancy because they impair cartilage development in animal studies	
Tetracycline	NOT recommended because it leads to discoloration of deciduous teeth	

Keep in mind that serum and tissue drug concentrations may be lowered secondary to physiologic changes of pregnancy including increased maternal fluid volume, drug distribution to the fetus, increased renal blood flow and associated increased glomerular filtration rate.

First line antibiotic choice is Ampicillin plus Gentamicin or Cephalosporins; 95% of women should respond within 72 hours.

The patient's symptoms are significantly improved within 24 hours and final urine cultures show pan-sensitive E coli.

What is your next step in management?

She should be treated with a 2-week course of outpatient oral antibiotics based on culture results. Consider suppressive therapy until delivery with 50–100 mg of nitrofurantoin nightly. If she elects against daily prophylaxis, she should be monitored closely throughout the remainder of her pregnancy for asymptomatic bacteriuria.

Why is the incidence of pyelonephritis increased in pregnancy?

The incidence of bacteriuria in pregnant women is similar to non-pregnant women; however, the incidence of acute pyelonephritis is increased due to physiologic changes associated with pregnancy.

Increased progesterone causes smooth muscle relaxation and dilation of the renal pelvis and ureters beginning in the seventh week. This leads to decreased peristalsis and urinary stasis.

Mechanical obstruction of the ureters is caused by a growing uterus, particularly on the right side. Approximately 20–40% of women with untreated bacteriuria will develop pyelonephritis during pregnancy, most commonly in the third trimester.

What are complications of untreated pyelonephritis in pregnancy?

1. Fetal prematurity
2. Low birth weight
3. Premature labor
4. Fetal mortality

CHAPTER 17

URETHRAL OBSTRUCTION

AARON BRAFMAN, MD
PETER CAI, MD
LAWRENCE YEUNG, MD

CASE 1

HPI 37-year-old Caucasian male farmer is referred to your clinic by his primary care physician for microscopic hematuria on 2 urinalyses over the last couple of months. He resides in a rural community a few hours away and just recently began receiving primary care. He discloses that he has had right sided discomfort over the last 5 years when drinking alcohol or large amounts of fluids. He describes the discomfort as colicky, 2 out of 10 in severity, and radiating to his groin. Occasionally he will take ibuprofen for the discomfort but does not notice any improvement. He denies fever, chills, nausea, and vomiting. No history of kidney stones, UTI, gross hematuria, or lower urinary voiding dysfunction.

PMH: none

PSH: tonsillectomy; circumcision

Allergies: NKDA **Medications:** occasional Ibuprofen

FH: none
SH: (-) tob; occasional ETOH; farmer
ROS: non-contributory

PE:

Vitals	T 98.6	BP 160/90	P 90	RR 12
Abdomen	soft; NT/ND			
Flank	mild (R) CVAT			
GU	normal circumcised phallus; adequate meatus; (B) testicles WNL			
Prostate	25 g; smooth and benign			
Rectal	benign			
Ext	(-) CCE			

As part of the initial hematuria workup, the primary care physician ordered an IVP at a local radiology center that showed (R) hydronephrosis with dilation of the (R) proximal ureter while the (R) distal ureter was not visualized. The (L) collecting system was normal.

What is your differential diagnosis at this point?

37-year-old CM with microscopic hematuria and symptomatic (R) proximal hydroureteronephrosis.

Acquired:
  Extrinsic: ureteral stone, peripelvic cyst or mass
  Intrinsic: benign fibroepithelial polyp, urothelial malignancy, post-inflammatory or post-operative scarring or ischemia
Congenital: retrocaval ureter, aperistaltic ureteral segment, mucosal kink/valve/adhesion

What initial lab tests do you order?

CBC → WNL
Chem 7 → WNL
UA → 10 RBC/HPF

What initial workup would you also obtain with the above labs?

Cystoscopy with retrograde pyelogram (RPG) and possible stent placement and CT Urogram

Cystoscopy with RPG:	normal bladder, (R) retrograde pyelogram shows an S-shaped deformity and proximal hydronephrosis; (-) filling defect Placement of (R) internal JJ stent resolves symptoms
CTU:	findings consistent with retrograde pyelogram: retrocaval ureter; (-) filling defect and no evidence of upper tract malignancy

What is your working diagnosis at this time?

37-year-old CM with microscopic hematuria and symptomatic (R) hydronephrosis and dilated proximal ureter on IVP likely secondary to (R) retrocaval ureter.

What is your next step?

The patient needs a transperitoneal dismembered ureteroplasty with transposition of the ureter, with stent and drain placement.

Discuss your surgical technique.

1. Place a Foley catheter
2. Supine position
3. Anterior midline incision
4. Transperitoneal dissection
5. Mobilize the proximal ureter/UPJ
6. Divide the ureter above and below the inferior vena cava (IVC), leaving enough redundancy to perform ureteroureterostomy
7. Reconstruct the ureter anterior to IVC
8. Perform the anastomosis
    a. Anastomosis should be water tight, tension-free, and widely patent
    b. Stent
9. Place a drain
10. Close the incision

What is the pathophysiology of retrocaval ureter?

Failure of supracardinal vein to develop into the IVC below the kidney possibly due to either persistence of subcardinal vein or persistence of posterior cardinal vein as the infrarenal IVC. Because this is due to a congenital abnormality of the vena cava, it can also be referred to as preureteral vena cava.

Overall incidence of approximately 1 in 1,100 with the majority of cases in male and involving the right ureter in the third or fourth decade of life. Common presenting symptoms include abdominal/flank pain, recurrent urinary tract infections, and hypertension.

CASE 2

HPI: 55-year-old Caucasian male presents with a complaint of (B) flank pain for the last 3–4 years. The flank pain has been getting worse in the past 3 months. He denies radiation, fever, nausea, vomiting, or other associated symptoms. He has no history of kidney stones, cancer, UTIs or gross hematuria. He denies obstructive or irritative voiding symptoms and has never had his PSA checked.

PMH: migraine headaches

PSH: RIH repair, appendectomy

Allergies: NKDA **Medications:** Methysergide (for migraine headaches)

FH: (-) urologic cancer or stones
SH: (+) tob; (+) ETOH
ROS: non-contributory

PE:

Vitals	T 98.6	BP 160/90	P 90	RR 12
HEENT	benign			
Abdomen	soft; NT/ND; well healed surgical incisions			
Flank	mild (B) CVAT			
GU	normal circumcised phallus; adequate meatus; (B) testicles WNL			
Prostate	25 g; smooth and benign			
Rectal	normal			
Neuro	non-focal			

What initial lab tests do you order?

CBC → WBC 10 k/μL; Hgb 13 g/dL; HCT 39%
Chem 7 → Na 140 meq/L; K 4.0 meq/L; Cl 100 meq/L; CO2 24 meq/L; BUN 10 meq/L; Cr 1.7 meq/L
UA → WNL
UCx → no growth
PSA → 1.0 ng/mL

What initial X-ray studies would you obtain?

Renal US: (B) hydroureteronephrosis

KUB: (-) kidney or ureteral stones

CT scan abdomen/pelvis: (B) hydronephrosis; (B) proximally dilated ureters to the level of the mid-ureter; medial deviation at L4-5 vertebral level, fibrotic retroperitoneal plaque with encasement of ureters and great vessels

What is your assessment?

55-year-old CM with bilateral hydronephrosis and suspected retroperitoneal fibrosis.

What is your differential diagnosis?

The differential diagnosis includes lymphoma, metastatic disease (of unknown primary including testicular cancer) and a primary retroperitoneal mass. While the CT findings (proximal hydroureteronephrosis, medial deviation of the ureters and extrinsic compression with fibrotic plaque) are classic, they do not rule out other etiologies that need to be ruled out.

How would you proceed?

Cystoscopy: normal bladder and urethra

(R) retrograde pyelogram: medially deviated ureter; small amount of contrast traverses proximal to mid ureteral extrinsic compression
(L) retrograde pyelogram: medially deviated ureter; small amount of contrast traverses proximal to mid-ureteral extrinsic compression

You successfully place internal JJ stents bilaterally. Monitor for post-obstructive diuresis. Monitor for normalization of serum creatinine and resolution of hydronephrosis and pain. If there is no improvement, consider PCN placement.

What are additional laboratory studies that may be abnormal in retroperitoneal fibrosis?

Erythrocyte sedimentation rate (ESR) and gamma globulin levels (IGg4) may be elevated.

What is your next step?

If there is a discrete mass, consider CT guided needle biopsy before exploratory laparotomy.

Needle biopsy: tissue with acute and chronic inflammatory changes; no evidence of malignancy.

What are the medical treatment options?

1. Glucocorticoids
   a. Considered a first-line agent
   b. Appear to be more effective in patients with laboratory evidence of active inflammation
   c. The best dose and length of treatment have not been established; a typical dose is 20–60 mg Prednisolone QOD × 6–8 weeks, then taper to 5 mg QOD for a total treatment period of up to 24 months if patient responds
   d. May be combined with other immunosuppressants such as Azathioprine, oral or IV Cyclophosphamide, Penicillamine or Mycophenolate mofetil
   e. Combine with H_2-blockers and Ca^{2+} supplements
2. Tamoxifen
   a. Alternative agent if steroids fail
   b. Anti-estrogen that is also effective in desmoid tumors characterized by locally invasive fibrous tissue
   c. Suggested dose is 20 mg PO QD × 12 months as monotherapy or sequentially after corticosteroids

You treat the patient with 8 weeks of 40 mg Prednisolone QOD. During that time he gains 20 pounds, develops signs of diabetes and feels miserable. Repeat CT scan shows a retroperitoneal mass of increased size. The patient is not interested in further conservative measures and wishes definitive surgical therapy.

What do you do next?

Discuss open surgical ureterolysis with him, including risks and complications.
Obtain informed consent.
Allow for enough time to taper his steroids before his surgery date.
Obtain preop labs, give bowel prep and have blood available.
Give preoperative antibiotics.

Discuss your surgical technique:

The Operation: Bilateral ureterolysis

1. Place NGT and Foley catheter
2. Midline incision from xiphoid to pubis
3. Inspect and palpate all 4 quadrants for malignancy
4. Take multiple deep wedge biopsies with intraoperative frozen section
    a. Frozen section: desmoplastic fibrous tissue
5. Identify the junction of dilated ureter and normal ureter
6. Ureter is easier to identify over the iliacs and is less involved here
7. Incise the posterior peritoneum
    a. Dissection should begin over the distal non-dilated ureter and proceed proximally to avoid injury of the thin dilated proximal segment
8. Dissect out the ureter sharply and bluntly
    a. Ureter may be managed in several ways:
        i. Move the ureter more laterally and secure the overlying peritoneum to maintain the ureters in this location
        ii. Place the ureter anteriorly into the peritoneal cavity with closure of the peritoneum behind it
        iii. If more extensive: wrap the ureter with a flap of omentum along its entire length. To do so, mobilize the omentum from its attachment to the transverse colon and divide along midline. Divide and ligate short gastric vessels so that the omentum can be swung laterally based on right and left gastroepiploic arteries
        iv. Close the incision

He underwent (B) ureterolysis with omental wrapping.

What is your post-operative care plan?

Ureteral stents should remain in place for 6 weeks until post-operative inflammation has subsided.

Discuss post-operative complications:

1. Ureteral injury
    a. Most important complication is injury to the ureter at the time of surgery
    b. Indwelling stents are most helpful to guide the dissection

    c. Proceed carefully, avoid excessive traction, and begin in a non-dilated portion of the ureter
    d. Unrecognized ureteral injuries can lead to complications and promote recurrent obstruction
2. Intestinal obstruction
3. Recurrent ureteral obstruction
    a. Post-operative use of corticosteroids may decrease risk of recurrent retroperitoneal fibrosis; need to balance risks and benefits on an individual basis
4. Post-obstructive diuresis
    a. May occur in patients with long-term (bilateral) obstruction who did not undergo prior stent or PCN placement
    b. Monitor for excessive urine output
    c. Replace IVF and electrolytes as necessary

What are surgical alternatives if ureterolysis is not feasible?

If diseased ureteral segments need to be excised, treatment options include ureteroneocystostomy with or without psoas hitch, Boari flap, ileal interposition, or kidney autotransplantation.

If no recovery of renal function occurs after a suitable length of decompression and the contralateral side is not involved and has adequate function, nephrectomy may be considered.

How do you follow-up?

Pathology: idiopathic tissue; (-) malignancy

Periodic follow-up with erythrocyte sedimentation rate (ESR) and BUN/Cr. Follow-up imaging with renal imaging (ultrasound, IVP, or CT scan) and renal scan to assess drainage.

What are the known causes of retroperitoneal fibrosis?

1. Drugs
    a. ß-blockers
    b. Methyldopa, Hydralazine
    c. Ergotamine alkaloids (LSD, Methysergide)
    d. Haloperidol
    e. Amphetamines
    f. Phenacetin
    g. Risperidone
2. Infection (syphilis, tuberculosis, gonorrhea, chronic UTI)
3. Chemicals (asbestos, talcum powder, Avitene)
4. Malignancy (primary, carcinoid or metastatic retroperitoneal tumors)

CASE 3

HPI: 25-year-old Caucasian female medical student presents to your clinic with complaints of left flank pain. She states that the pain first started 3 years ago and is intermittent, colicky, non-radiating and can be 8 out of 10 in severity, especially after drinking a lot of fluids or alcohol. While she does get some mild nausea with these episodes, she denies any fever, chills, or vomiting. She has no other voiding complaints and no history of stones or tumors.

PMH: none; last menses 3 weeks ago; no possibility of pregnancy

PSH: none

Allergies: NKDA **Medications:** oral contraceptive pills

FH: none
SH: (-) tob; (-) ETOH; medical student
ROS: (-) except for above

PE:

Vitals	T 98.6	BP 140/60	P 90	RR 12
Abdomen	soft; NT/ND			
Flank	mild left CVAT			
Pelvic	external genitalia unremarkable			
Rectal	benign			
Ext	(-) CCE			
Neuro	non-focal			

Labs:

CBC	→	WBC 9 K/μL; Hgb 12 g/dL; HCT 36%
Chem 7	→	Na 140 meq/L; K 4.0 meq/L; Cl 100 meq/L; CO2 24 meq/L; BUN 10 mg/dL; Cr 1.3 mg/dL
UA	→	WNL
bHCG	→	negative for pregnancy
Renal US:		left moderate/severe hydronephrosis with cortical thinning, normal right kidney, ureters not visualized bilaterally.

What is your assessment?

25-year-old CF with intermittent left flank pain with associated hydronephrosis. This is likely a chronic process given the cortical thinning.

What is your next step?

Since renal US is abnormal, you must proceed with further imaging to evaluate for obstruction. Consider a VCUG (unlikely to have reflux with no ureteral dilation seen on renal US).

VCUG:	(-) vesicoureteral reflux bilaterally
DTPA diuretic renogram:	(L) 35% function; T½ → 25 min (R) 65% function; T½ → 5 min
CT:	moderate/severe left hydronephrosis without hydroureter, large amount of extrarenal pelvis present, no renal stones or other abdominopelvic abnormalities seen

What is your working diagnosis at this time?

25-year-old CF with intermittent left flank pain likely secondary to a congenital left UPJ obstruction.

How would you counsel this patient?

This patient needs reconstruction of her left ureteropelvic junction. She has enough remaining renal function to justify repair. This can be performed endoscopically (endopyelotomy) or open/laparoscopically (pyeloplasty).

Discuss the surgical technique of an endopyelotomy and pyeloplasty.

1. Endopyelotomy (antegrade/retrograde): make a longitudinal incision in a posterolateral direction at the UPJ (to avoid injuring a possible crossing vessel) under ureteroscopic vision until you see periureteral fat. Leave a stent for 6 weeks.
2. Pyeloplasty (open/laparoscopic/robotic)
    a. Anderson-Hynes dismembered pyeloplasty
        i. Excise redundant pelvis and remove stenotic UPJ and create a tension-free, water tight anastomosis in a dependent location
    b. Foley Y-V pyeloplasty
        i. Useful for high insertion of the ureter
    c. Spiral flap (Culp-Deweerd) pyeloplasty
        i. Useful in redundant pelvis and long UPJ stricture
    d. Vertical flap (Scardino) pyeloplasty
        i. Useful in redundant pelvis and long UPJ stricture

You proceed with a laparoscopic dismembered pyeloplasty without complications.

How would you follow-up?

Follow-up with BUN/Cr and renogram approximately 2 months after the ureteral stent has been removed.

What are her treatment options if she develops recurrent UPJ obstruction?

Consider that she may need to be worked up with an antegrade nephrostogram and a retrograde pyelogram to define the extent of the obstruction.

The choice of procedure depends on stricture length and intraoperative findings:

1. Salvage endopyelotomy

2. Re-do pyeloplasty
3. Ureterocalicostomy
    a. Reasonable procedure if the renal pelvis is small and primary anastomosis between the ureter and the renal pelvis cannot be performed
4. Ileal ureter
    a. Reasonable technique if no contraindication and long segment stricture
    b. Patient needs to have decent renal function (typically Cr below 1.8–2.0) to prevent electrolyte abnormalities
5. Autotransplantation
    a. If none of the above are feasible or chosen by the patient, autotransplantation may be necessary
6. Nephrectomy
    a. Indication for a simple nephrectomy is non-function (<15% function) of the affected kidney in the presence of a normal contralateral kidney
    b. Simple nephrectomy is also a consideration when prior repairs have failed and further attempts would be extremely complicated. Additional indications include short life expectancy due to advanced age or co-existing complex medical problems

She develops recurrent UPJ obstruction with maintained renal function.
She consents to undergo re-do pyeloplasty.

Upon inspection, you see the renal pelvis is very small and the proximal ureter is encased in a scar and the lower pole is severely dilated with little overlying parenchyma.

What do you do at this point?

Proceed with a ureterocalicostomy.

Discuss your surgical technique.

1. Amputate the lower pole of the kidney
2. Mobilize the lower pole calyx
3. Excise strictured ureter
4. Spatulate the ureter
5. Obtain watertight tension free anastomosis of the ureter and the calyx
6. Insert a stent
7. Wrap omentum, peritoneum, or perirenal fat around the anastomosis
8. Place a drain

She tolerates the procedure well without complications and recovers well with preserved renal function.

CASE 4

HPI: 54-year-old Asian male who recently immigrated to the US is referred to your clinic for persistent dysuria along with multiple urinalyses that show microscopic hematuria, proteinuria, and pyuria with negative cultures. He states that he has had dysuria for approximately 8 years but has never developed systemic symptoms such as fever, nausea, or vomiting. No history of kidney stones, culture-proven UTI, gross hematuria, or other urinary tract disease.

PMH: HTN; DM; BPH; most recent PSA 3.2; active tuberculosis diagnosed 2 months ago with documented sputum conversion

PSH: cholecystectomy, TURP 4 years ago

Allergies: none

Medications: Isoniazid, Rifampin, Pyrazinamide, Ethambutol, Tamsulosin

FH : esophageal cancer in father at age 57
SH: (-) tob; (+) ETOH 3 drinks/week; retired car mechanic from China currently living with his son who is a pharmacist
ROS: non-contributory

PE:

Vitals	T 99.4	BP 153/91	P 85	RR 16
Lungs	CTAB			
Abdomen	soft; NT/ND			
Flank	mild (R) CVAT			
GU	normal circumcised phallus; adequate meatus;(B) testes WNL			
Prostate	40 g; smooth and benign, nontender			
Rectal	benign			
Ext	(-) CCE			
Neuro	non-focal			

What is your differential diagnosis at this point?

54-year-old AM with chronic dysuria, microscopic hematuria, proteinuria, and sterile pyuria possibly from urinary tract malignancy, BPH, prostate cancer, prostatitis, urolithiasis or UTI.

What initial lab tests do you order?

CBC → WNL
Chem 7 → Creatinine elevated at 1.3
UA → 10 RBC/hpf, 100 WBC/hpf

What other workup would you obtain with the above labs?

Cystoscopy: normal bladder, prostate with TUR defect and minimal regrowth adenoma

CTU: Multiple 2 to 3 mm calcifications along the distal left ureter and ureterovesical junction with significant ureteral narrowing and moderate hydroureteronephrosis proximal to these lesions; no evidence of upper tract malignancy

Urine culture for AFB: + Mycobacterium tuberculosis

What is your working diagnosis at this time?

54-year-old AM with lower urinary tract symptoms and distal ureteral stricture secondary to ureteral tuberculosis.

What is your next step?

The patient needs left upper tract decompression with either a ureteral stent or percutaneous nephrostomy tube.

How do you proceed?

Obtain adequate follow-up for symptoms and renal function during the next 4 months as patient completes his 6-month regimen of treatment for active tuberculosis. His Cr trends down to 0.8.

Consider that clinical response to tuberculosis medications is generally favorable due to high urinary concentrations, but symptoms of urinary tract obstruction during treatment can suggest progression of strictures secondary to scarring and narrowing of the lumen.

How do you proceed following completion of medical treatment?

You counsel the patient on ureteroscopic evaluation. You note a 6–7 cm narrowing of the distal (L) ureter beginning at the ureterovesical junction with fibrotic change and multiple biopsies are obtained.

It is important to assess not only the ureter, but the kidney as well. Renal TB is the most common site of GU TB and ureteral manifestations are secondary to a “trickle-down” effect. Those with renal involvement typically have infundibular stenosis and papillary necrosis.

Biopsies confirm fibrosis, likely secondary to ureteral TB. No renal or upper ureteral involvement is noted.

What are the options for management of distal ureteral strictures?

Endourologic options: stent placement, retrograde balloon dilation, antegrade balloon dilation, and endoureterotomy

Surgical reconstruction: ureteroureterostomy, transureteroureterostomy, ureteroneocystostomy, ileal ureter, autotransplantation

Ureteroureterostomy is most appropriate for short defects of the upper or midureter. Distal ureteral strictures are best managed with ureteroneocystostomy with or without a Boari flap and/or psoas hitch. Ileal ureter and autotransplantation should be considered for very long strictures or after other methods have failed or are not feasible due to complications involving infections, stones, metabolic abnormalities, and risk for loss of the ipsilateral kidney.

Consider that for both psoas hitch and Boari flap, preoperative evaluation of bladder function and capacity, bladder outlet obstruction and neurogenic dysfunction should be addressed before performing the procedure.

Describe the steps to performing open ureteroneocystostomy with Boari flap.

1. Place a Foley catheter sterilely on the field
2. Supine position
3. Midline incision
4. Identify the distal ureter as it crosses the iliac vessels
5. Preserve adventitia to maximize post-operative blood supply
6. Can perform flexible ureteroscopy via urethra to help identify distal extent of stricture. Transect at level of obstruction and mobilize proximally
7. Perform ureteroneocystostomy only if tension-free anastomosis is possible; if not, psoas hitch or Boari flap should be used
8. Divide contralateral bladder pedicle for improved mobility on ipsilateral side
9. Posterolateral bladder flap outlined based on identification of ipsilateral superior vesicle artery supply
10. Distal end of flap should be pexed to psoas minor tendon or psoas major muscle with absorbable suture
11. Distal ureter should be spatulated and anastomosis is performed
12. Remaining bladder flap is tubularized and closed
13. Prior to closing bladder flap, leave JJ stent in place post-operatively for anastomosis to heal
14. Place closed suction drain in pelvis
15. Leave urethral catheter in place post-operatively to minimize bladder filling pressures

CASE 5

HPI: You receive a consult on a 4-year-old Caucasian male admitted with left-sided flank pain with associated nausea and vomiting. His parents report that his symptoms started 3 days ago, and he has never had any prior episodes.

PMH: none

PSH: bilateral tympanostomy tubes

Allergies: none **Medications:** none

FH: non-contributory
SH: lives at home with parents
ROS: non-contributory

PE:

Vitals	T 99.4	BP 94/68	P 91	RR 19
GA	WDWN CM INAD			
HEENT	benign			
Heart	RRR			
Lungs	CTA			
Abdomen	soft; right-sided tenderness; nondistended			
Flank	mild (L) CVAT			
GU	normal circumcised phallus; orthotopic meatus; (B) testes WNL			
Ext	(-) CCE			
Neuro	non-focal			

Labs:

CBC → normal
BMP → Cr 1.2
UA → normal

Imaging:

Renal US: left hydroureteronephrosis with a cystic dilation within the bladder lumen

Mag-3 Lasix renogram: (L) kidney 32% diff function, (R) kidney 68% diff function; t1/2 72 minutes (L), t1/2 6 minutes (R)

What is your assessment?

4-year-old CM with left-sided hydroureteronephrosis secondary to an obstructing ureterocele.

What is your next step in management?

You counsel the family on cystoscopy and incision of ureterocele. Cystoscopy is performed and upon entry of the bladder, no ureterocele is identified. Upon further inspection, you note extrinsic left posterior bladder wall compression. The left ureter is cannulated and a retrograde pyelogram is performed. The ureter is massively dilated and the contrast does not drain into the bladder. A ureteral stent is placed.

What is your new assessment?

4-year-old CM with an obstructed megaureter or UVJ obstruction.

What is the most common pathology that results in an obstructed megaureter?

An adynamic distal ureteral segment.

What are the options for operative approaches?

1. Distal cutaneous ureterostomy (temporary diversion)
2. Tapered ureteral reimplantation (definitive management)

You proceed with a tapered ureteral reimplantation.

What are the principles you must consider?

1. Create a smooth transition from proximal ureter to the tapered segment
2. Ureter is loosely tapered over a 10–12 Foley catheter
3. Be mindful of devascularization when choosing the ureteral segment to excise
4. Mucosa-mucosa apposition with ureteral closure
5. 4:1 to 5:1 ratio of tunnel length to ureteral diameter for an antirefluxing repair
6. Ureteral stent placement
7. Foley catheter placement
8. Prophylactic antibiotics

The patient does well postoperatively and the ureteral stent is removed 1 week later.

What is your follow up plan?

Post-operative ureteral edema persists for 4–5 weeks, so a renal US and/or renal scintigraphy is performed 6 weeks postoperatively. Hydronephrosis has improved and there is no evidence of obstruction on renal scan.

CHAPTER 18

UROLOGIC TRAUMA

JAMES MASON, MD
LAWRENCE YEUNG, MD

CASE 1

HPI: 54-year-old Caucasian male involved in a pedestrian and motor vehicle accident presents to the emergency department. The paramedic informs you the patient had no loss of consciousness. EBL is unknown. The patient has not voided since the accident.

PMH: GERD

PSH: appendectomy

Allergies: none **Medications:** Prilosec

FH: non-contributory
SH: (-) tob; (-) ETOH
ROS: (+) pelvic pain

PE:

Vitals	T 98.6	BP 90/40	P 130	RR 16
General Exam	fully-developed adult CM in acute distress			
HEENT	benign			
Heart	sinus tachycardia			
Lungs	CTA			
Abdomen	soft; moderate tenderness; (+) suprapubic distention; unstable and tender pelvis			
Flank	(-) CVAT; (-) ecchymosis			
GU	normal circumcised male; blood at meatus; bilateral testicles WNL; butterfly ecchymosis of the perineum			
Prostate	high riding prostate			
Ext	(-) CCE; (-) fractures; good pedal pulses			
Neuro	non-focal; responds well to commands			

What is your first measure of action?

Initiate trauma ABCDE's. Also known as the primary survey.

A = Airway with c-spine protection
B = Breathing
C = Circulation, stop bleeding
D = Disability/Neuro status
E = Exposure and Environment

As you do the primary survey you should send off trauma labs and obtain imaging while stabilizing the patient.

Labs include Chem 18, CBC, PT/PTT, ABG, T&C, Toxicology screen, UA. Imaging generally includes C-spine, CXR, KUB, and bedside FAST (focused assessment with sonography in trauma).

If the patient is unconscious, a nasogastric tube should be placed along with endotracheal tube. Typically, a urethral catheter would be placed, but since he has blood at the meatus, a urethra catheter insertion should not be attempted at this time.

Chem 18	→	Cr 1.0, remainder normal
CBC	→	WBC 11,000, Hgb 9 g/dL, Hct 27%
PT/PT	→	WNL
ABG	→	WNL
Tox Screen	→	(+) ETOH
C-spine	→	normal, all 7 vertebrae visualized
CXR	→	normal; (-) pneumothorax; (-) rib fractures
KUB	→	open-book pelvic fracture; fractured pubic ramus
FAST	→	WNL

The trauma surgeons stabilize the pelvic fracture with MAST trousers.

What is the next step?

Obtain a retrograde urethrogram prior to placing a urethral catheter.
Also obtain CT abdomen/pelvis to fully evaluate extent of pelvic and abdominal injuries.

RUG	→	urethral disruption with extravasation of contrast; there is no opacification of the posterior urethra
Abdominal CT	→	normal
Pelvic CT	→	multiple pelvic fractures

Describe how to perform a retrograde urethrogram.

1. Insert cone tipped 60 cc syringe or Foley catheter with balloon inflated with 1–2 mL fluid within the fossa navicularis
2. Position penis at a 90° angle to body and oblique patient or the fluoroscope 45°
3. Slowly inject contrast

You perform the RUG and contrast does not pass proximal to what appears to be the proximal bulbar urethra.

What is your assessment?

54-year-old CM with a pelvic fracture urethral distraction defect (PFUDD) and urinary retention.

What are the treatment options?

1. Pass urethral catheter—DO NOT attempt this blindly in the presence of urethral disruption
2. Primary realignment of the urethra in the OR
3. Suprapubic tube placement at the bedside

If the patient is going to the OR for other injuries, an endoscopic realignment may be attempted. Long term success of primary realignment is < 20%.

Also, primary endoscopic realignment may be associated with more endoscopic interventions and longer time to definitive resolution than open realignment or SP tube placement.

You chose bedside suprapubic tube placement.

What should you perform next?

You would send a urine culture and perform a cystogram via the suprapubic tube.

Describe how to perform a cystogram.

Fill the bladder with 300–400 mL of contrast under gravity or until patient cannot tolerate any more contrast in bladder.

Cystogram shows an intraperitoneal bladder rupture.

What do you do now?

1. You would perform an exploratory laparotomy to repair the bladder rupture
2. You should also inspect the bowel and other abdominal organs (liver, spleen) for injury
3. If there is pelvic hematoma, you should avoid opening this due to the risk of intractable bleeding

At the time of exploration, your partner opens the pelvic hematoma against your advice and there is profuse bleeding.

How do you manage this?

1. Pack the pelvis
2. Inform the anesthesiologist of ongoing blood loss. Transfuse as necessary
3. Consult orthopedics for pelvic fracture fixation

If the bleeding does not stop, packing the pelvis and closing the abdomen with return to the OR in 24–48 hours may be necessary. Can also consider Interventional Radiology consult for embolization if possible.

The bleeding was controlled in the OR with packing.

What do you do next?

Repair the bladder injury.

Discuss your technique for bladder injury repair.

1. Once injury is identified, close with absorbable sutures in 2 layers
2. If location of injury is not immediately obvious, make cystotomy at the dome
3. Inspect bladder interior, identify ureteral orifices
4. Place pelvic drain to monitor post-operatively for possible leak

During the bladder repair, you decide to perform simultaneous antegrade and retrograde cystoscopy to attempt primary realignment of the urethra. You were able to successfully place a urethral catheter over a guidewire across the urethral injury and removed the suprapubic tube.

The patient is discharged in 1 week with the urethral catheter.

What is your follow up plan?

1. Keep the urethral catheter for 4 weeks. Perform a peri-catheter retrograde

urethrogram prior to removal

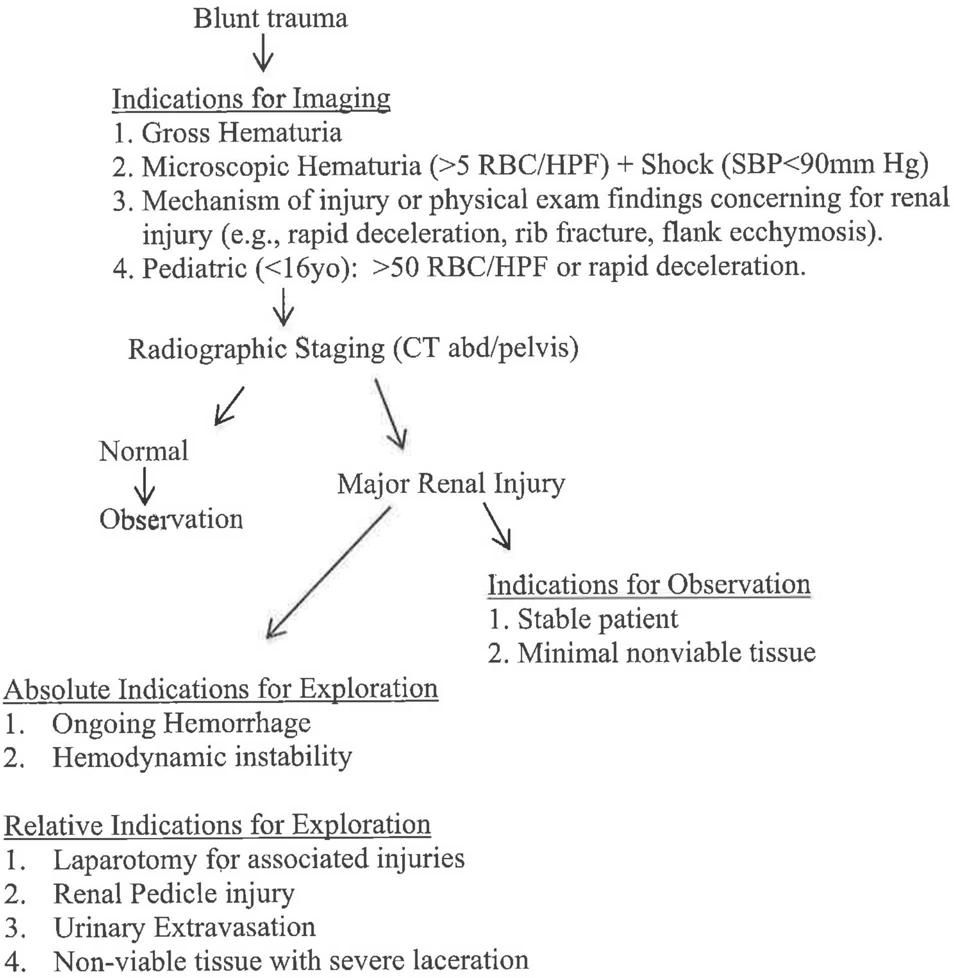
2. Perform cystogram to ensure bladder perforation is healed (if there was no urethral injury then bladder injury could have been managed with cystogram and catheter removal at 2 weeks)
3. You perform a peri-catheter RUG and cystogram and there is no extravasation

He returns to see you in clinic in 3 months and is voiding well with normal erections and no problems with urinary incontinence and thanks you.

Describe some possible complications of posterior urethral injury.

1. Impotence
2. Urinary incontinence
3. Urethral stricture

Describe the genitourinary blunt trauma algorithm.



Blunt trauma

Indications for Imaging
1. Gross Hematuria
2. Microscopic Hematuria (>5 RBC/HPF) + Shock (SBP<90mm Hg)
3. Mechanism of injury or physical exam findings concerning for renal injury (e.g., rapid deceleration, rib fracture, flank ecchymosis).
4. Pediatric (<16yo): >50 RBC/HPF or rapid deceleration.

Radiographic Staging (CT abd/pelvis)

Normal

Observation

Major Renal Injury

Indications for Observation
1. Stable patient
2. Minimal nonviable tissue

Absolute Indications for Exploration
1. Ongoing Hemorrhage
2. Hemodynamic instability

Relative Indications for Exploration
1. Laparotomy for associated injuries
2. Renal Pedicle injury
3. Urinary Extravasation
4. Non-viable tissue with severe laceration

Describe the different types of urethral injuries.

Goldman classification of urethral injuries (updated Colapinto scale)

Type 1: rupture of puboprostatic ligaments and periprostatic hematoma stretch membranous urethra without rupture

Type 2: partial or complete rupture of membranous urethra above urogenital diaphragm

Type 3: partial or complete rupture of membranous urethra with disruption of urogenital diaphragm
Type 4: Bladder neck injury with extension into the urethra
Type 4a: Extraperitoneal bladder rupture at bladder base with periurethral extravasation
Type 5: Pure anterior urethral injury

Describe urethral injury grading based on the American Association for the Surgery of Trauma (AAST) scale.

Grade	Injury Type	Description
I	Contusion	Blood at meatus, normal RUG
II	Stretch Injury	Elongation of urethra, no extravasation on RUG
III	Partial Disruption	Extravasation on RUG at injury site with contrast visualized in the bladder
IV	Complete Disruption	Extravasation on RUG at injury site without contrast visualized in bladder, <2cm of urethral separation
V	Complete Disruption	Complete transection with >2cm urethral separation or extension into the prostate or vagina

Moore E, Cogbill T, Jurkovich G, et al. Organ injury scaling III: chest wall, abdominal vascular, ureter, bladder, and urethra. J Trauma & Acute Care Surg 1992(3);337–9. Table 5. Copyright © 1992, Williams. Used with permission.
Online at http://www.aast.org/Library/TraumaTools/InjuryScoringScales.aspx#blatter (Table 22 Urethra Injury)

CASE 2

HPI: You are consulted by Trauma Surgery regarding a 35-year-old male involved in a fall >20 feet from a building. He has evidence of pelvic fracture and voided gross blood on arrival to the trauma bay. A urethral catheter insertion has been deferred pending your evaluation.

PMH: none

PSH: none

Allergies: NKDA **Medications:** none

FH: non-contributory
SH: (-) tob; (-) ETOH
ROS: non-contributory

PE:

Vitals	T 98.6 BP 90/40 P 130 RR 16
GA	adult M, in acute distress
HEENT	benign
Heart	sinus tachycardia
Lungs	decreased breath sounds on right; multiple rib fractures on right; normal breath sounds on left
Abdomen	soft; moderate tenderness; (-) suprapubic distention; unstable and tender pelvis
Flank	(+) right CVAT; (+) right ecchymosis
GU	normal circumcised male; no blood at meatus; bilateral testicles WNL; no butterfly ecchymosis of the perineum
Prostate	small anodular prostate; no blood
Ext	(-) CCE; right femur fracture; good pedal pulses
Neuro	non-focal; responds well to commands

Labs:

Chem 18 → WNL
CBC → WBC 9 K/μL, Hgb 9 g/dL, HCT 27%
PT/PT → WNL
ABG → WNL
Tox Screen → (+) ETOH
C-spine → normal, all 7 vertebrae visualized
CXR → right pneumothorax, right rib fractures
KUB → open-book pelvic fracture, fractured pubic ramus
Leg X-Ray → compound right femur fracture
FAST → WNL

A right sided chest tube was placed by trauma surgery in the trauma bay.

What is your first step in further assessment?

Obtain a retrograde urethrogram before placing a urethral catheter. You also would obtain a CT abdomen/pelvis to fully evaluate his pelvic injuries and upper urinary system considering the mechanism of injury in addition to the rib fractures.

RUG → normal
Abdominal CT → right lower pole grade IV renal laceration with urine extravasation; normal left kidney and ureter; (+) right retroperitoneal hematoma; no other noted intra-abdominal injuries
Pelvic CT → multiple pelvic fractures

What is your next step?

You place a urethral catheter, send a urine for culture and sensitivity, and perform a cystogram (Remember that the patient voided gross blood on arrival to the trauma bay).

Cystogram → flame shaped extravasation of contrast seen from the bladder; no contrast outlining bowel.

What is your diagnosis?

Likely extraperitoneal bladder rupture.

Orthopedic Surgery plans to take the patient to the OR for pelvic and femur fixation.

How would you manage the renal injury and bladder injury in this situation?

Renal—there is no current indication to explore the fractured kidney.

Indications for renal exploration:

1. Hemodynamic instability from ongoing bleeding
2. Expanding pulsatile retroperitoneal hematoma
3. High grade injuries in solitary kidney
4. High velocity penetrating trauma

Bladder—the bladder should be repaired at the time of pelvic fixation.

Indications for bladder repair:

1. All intraperitoneal bladder perforations
2. Complicated extraperitoneal bladder ruptures (i.e., bone fragments intruding into bladder, bladder neck involvement, or concurrent rectal or vaginal laceration)
3. Extraperitoneal bladder ruptures in patients undergoing other intraabdominal/pelvic open surgical interventions (e.g., pelvic repair)

You repair the extraperitoneal bladder injury at the time of pelvic fixation.

Discuss your technique for bladder injury repair.

1. Once injury identified, close with absorbable sutures in 2 layers
2. If location of injury is not immediately obvious, make cystotomy at the dome
3. Inspect bladder interior, identify ureteral orifices
4. Place pelvic drain to monitor post-operatively for possible leak
5. Place large bore (i.e., 18 F) Foley catheter to maximize drainage of urine from bladder

On hospital day 2, he becomes hypotensive. He does not respond hemodynamically to resuscitation efforts (fluid boluses, blood transfusion). After 4 units of PRBC, his Hbg/HCT is 7 g/dl and 21%.

What is your next step?

If the patient is unstable, then he should go directly to the OR for right retroperitoneal exploration. If the patient is stable but has persistent bleeding with poor response to resuscitation, and a reliable Interventional Radiology team is available, then an attempt at embolization of the bleeding vessel is warranted.

You decide the patient is too unstable for minimally invasive therapy. You decide to go directly to the OR.

Discuss your surgical technique for renal exploration.

1. Supine position
2. Midline incision from xiphoid to pubis
3. Obtain vascular control without disturbing the retroperitoneal hematoma
   a. First place transverse colon onto the patient's chest under moist sponges
   b. Expose root of the small bowel mesentery by lifting small bowel superiorly to the right
   c. Make vertical incision over aorta (medial to inferior mesenteric vein) superior to IMA and extend upward to ligament of Treitz
   d. Identify aorta, dissect upward until the left renal vein is exposed. The left renal artery is just posterior to this
4. After vascular control is established, mobilize the left kidney
   a. Occlude the renal artery if needed (may also use manual compression of the kidney). Artery clamping >30 mins requires surface cooling with ice
   b. Sparingly debride all nonviable tissue
   c. Perform a partial nephrectomy if feasible or perform a simple nephrectomy
   d. Control active bleeding vessels
   e. Close collecting system with absorbable suture
   f. Close renal parenchyma over laceration
5. Close the renal parenchyma defect
   a. Close renal capsule over bolsters
   b. Close Gerota's fascia
   c. Place a drain near the retroperitoneum. Do not place drain directly over repaired site to avoid fistula formation

Assume you performed a lower pole hemi nephrectomy due to a devitalized lower pole.

Discuss possible intraoperative complications and management.

1. Splenic Injury—minor lacerations of the capsule may be treated with cautery and surgical or gelfoam
2. Pancreatic Injury—injuries to the tail of the pancreas require distal pancreatectomy
3. Intractable bleeding—heavy bleeding during partial nephrectomy may warrant simple nephrectomy
4. Bowel Injury—may require repair with primary closure (if small) or excision and primary anastomosis.

Discuss this patient's post-operative management.

1. Remove the drains when the output is minimal. Check drain for creatinine prior to removal if any concern for urine leak
2. Continue urethral catheter for 2 weeks to allow cystorrhaphy to heal
3. Obtain cystogram prior to removal of the urethral catheter

What are early post-operative complications of partial nephrectomy?

1. Delayed bleeding
    a. Need to work up for pseudoaneurysm with CT with IV contrast. If present, then send to interventional radiology for embolization
2. Urinoma
    a. Place internal ureteral stent and Foley catheter
    b. If it persists have IR place percutaneous drain
3. Perinephric abscess
    a. Evaluate for possible urinoma as source
    b. Have IR place percutaneous drain
    c. If abscess persists then open drainage may be needed

What are the late post-operative complications from partial nephrectomy?

1 UPJ obstruction
    a. occurs from excessive scarring around the renal hilum and UPJ
2. HTN
    a. Incidence of delayed HTN after renal trauma is 5%
    b. This is secondary to renal compression from hematoma (Page kidney) or increased renin production due to ischemic parenchyma
3. AVM (arteriovenous malformation)

What are absolute indications for abdominal exploration?

1. Ongoing hemorrhage
2. Hemodynamic instability
3. Ureteral injury and UPJ disruption
4. If patient is stable, can make attempt at primary repair
5. If patient is unstable, can temporize with nephrostomy tube or externalized ureteral stent secured to the proximal end of ureteral defect. Definitive repair then attempted when patient stable

How do you manage hemodynamically stable trauma patients with blunt Grade III renal trauma?

1. Obtain serial HCT
2. Monitor vitals
3. Bedrest and observation
4. Restrict physical activity until hematuria resolves

How do you perform a "one shot IVP" in a trauma setting?

Inject 2 mL/kg or maximum of 150 mL of IV contrast, wait 10 minutes and obtain plain abdominal radiograph.

What is the imaging of choice for low-velocity penetrating trauma?

CT scan of the abdomen and pelvis with IV contrast.

Describe the American Association for the Surgery of Trauma (AAST) renal injury scoring scale.

Grade	Type of Injury	Description
I	Contusion	Microscopic or gross hematuria, urologic studies normal
	Hematoma	Subcapsular, nonexpanding without parenchymal laceration
II	Hematoma	Nonexpanding perirenal hematoma confined to retroperitoneum
	Laceration	<1cm parenchymal depth of renal cortex
III	Laceration	>1cm parenchymal depth without collecting system rupture or urinary extravasation
IV	Laceration	Parenchymal laceration involving collecting system
	Vascular	Main renal artery or vein injury with contained hemorrhage
V	Laceration	Completely shattered kidney
	Vascular	Avulsion of renal hilum with devascularized kidney

Moore EE, Shackford SR, Pachter HL, et al: Organ injury scaling—spleen, liver, and kidney. J Trauma 29:337–9, 1989. Table III. Copyright © 1989, Williams. Used with permission.
Online at http://www.aast.org/Library/TraumaTools/InjuryScoringScales.aspx#blatter (Table 19 Kidney Injury)

CASE 3

HPI: You are called to the trauma bay to evaluate a 43-year-old male who sustained a gunshot wound to the lower abdomen. Paramedics provide information regarding the event. Apparently, the patient was walking down the street minding his own business and he was shot several times in the abdomen and pelvis by an unknown gunman. The gun used was a handgun of unknown caliber.

PMH: none

PSH: none

Allergies: NKDA **Medications:** none

FH: non-contributory
SH: (-) tob; (-) ETOH
ROS: non-contributory

PE:

Vitals	T 97.8	BP 97/60	P 110	RR 15
General Exam	adult M in acute distress			
HEENT	benign			
Heart	sinus tachycardia			
Lungs	CTA B			
Abdomen	ridgid; (+) guarding; multiple GWS to lower abdomen and pelvis			
Flank	(-) CVAT; (-) right ecchymosis; no bullet wounds			
GU	normal circumcised male; (+) blood at meatus; bilateral testicles WNL; no butterfly ecchymosis of the perineum			
Prostate	small anodular prostate, (+) heme			
Ext	(-) CCE, right femur fracture, good pedal pulses			
Neuro	non-focal, responds well to commands			

Labs:

Chem 18 → WNL
CBC → WBC 11 K/μL, Hgb 8g/dL, HCT 24%
PT/PT → WNL
ABG → WNL
Tox Screen → (+) ETOH; (+) marijuana
C-spine → normal; all 7 vertebrae visualized
CXR → WNL
KUB → bullet fragments in the right mid pelvis
FAST → WNL

Assuming the ABCDE's of the primary survey has been initiated, what is the next step in management?

CT abdomen and Pelvis → both kidneys intact, prompt excretion of both kidneys; left ureter seen down to bladder; right mid and distal ureter not opacified; 3 bullet fragments lodged in the right retroperitoneum and mid pelvis; there is free air within the abdomen

Note: If the patient is unstable, he should be taken directly to the OR for exploratory laparotomy.

What are the next steps in management?

Obtain a retrograde urethrogram since he has blood at the meatus and cystogram because there is concern for bladder perforation with low abdominal GSW.

RUG → normal; you place a catheter with return of gross blood; send a UA and culture
Cystogram → (+) intraperitoneal extravasation of urine

Note: In patients with gross blood return on catheter placement, a CT cystogram can be obtained. The bladder is filled with 300–400 mL of contrast by gravity through the Foley catheter or until the patient is uncomfortable.

What would you do next?

Take the patient to the OR with trauma surgery emergently for exploratory laparotomy.

How would you explore his pelvis injuries? Describe your technique.

1. Midline incision
2. Inspect all 4 quadrants: shows that kidneys, liver and spleen are normal
3. Run the entire bowel: he has 4 holes in the small bowel
4. Have trauma surgery repair the bowel
5. Inspect the right ureter: this shows the right mid ureter is torn from the blast injury
6. Repair the ureter by excising the devitalized portion
7. Spatulate the proximal and distal ends of the ureter
8. Perform a ureteroureterostomy with absorbable 4–0 or 5–0 suture; ensure good mucosal apposition, tension-free and water tight anastomosis
9. Place a double J stent prior to completing the anastomosis
10. Place drain in the retroperitoneum
11. Inspect the bladder: defect seen at dome of bladder and posterior bladder wall
12. Open the bladder at the dome and inspect the interior to identify any additional injuries
13. Both UO's are identified
14. Distal end of the JJ stent from the ureteral repair is in good position
15. A single bullet entrance is located at the dome, and a single exit wound is in the posterior bladder
16. You note fecal material on the posterior wall of the bladder and anterior to the rectum
17. Close the bullet defects and close the cystotomy: see CASES 1 & 2 for proper bladder closure
18. Inspect the rectum: this shows a large rectal wall defect

How would you repair the rectal defect if general surgery was not available?

1. Irrigate the wound
2. Excise the devitalized portion of the rectal wall
3. Close the rectal injury in anatomic layers
4. Create a diverting colostomy and Hartmann's pouch
5. Interpose omentum over the rectal repair

6. Place presacral drains
7. Bring out the presacral drains through the perineum

What is your post-operative plan for care?

1. NPO and NGT
2. Urethral catheter to drain
3. Broad spectrum antibiotics

What is your follow up plan?

1. Cystogram in 14 days
2. Remove ureteral stent in 6 weeks
3. Colostomy takedown after rectal injury has healed (3–6 months)

CASE 4

HPI: You are taking over hospital call from your partner for the week. Over the weekend, your partner managed a patient involved in a roll-over motor vehicle collision with a crush injury to the pelvis. A suprapubic tube was placed due to a pelvic fracture urethral distraction defect. The patient has been managed by the trauma service since for other serious injuries. The trauma service has called you to evaluate the patient due to new erythema and swelling of the perineum and scrotum.

PMH: IDDM

PSH: SPT

Allergies: PCN **Medications:** Insulin; narcotic pain medications

FH: non-contributory
SH: (-) tob; (+) ETOH
ROS: non-contributory

PE:

Vitals	T 101.6 BP 102/69 P 127 RR 18
General Exam	adult M in hospital bed; appears in moderate distress
HEENT	benign
Heart	sinus tachycardia
Lungs	CTA B
Abdomen	soft; ND, NT; SP tube draining dark yellow urine
Flank	(-) CVAT; (-) ecchymosis
GU	normal circumcised male; very tender erythema of the lower half of the scrotum and complete perineum; + crepitus of scrotum/perineum
Prostate	high riding prostate; no crepitus of rectal wall
Ext	(-) CCE
Neuro	non-focal; responds well to commands

Labs:

Chem 7 → Cr 1.2, glucose 280 meq/L, CO2 20 meq/L, K 3.5 meq/L
CBC → WBC 19 K/µL, Hgb 9g/dL, HCT 27%
PT/PT → WNL
UA → 2-3 RBC/HPF, 7-8 WBC/HPF, few bacteria
UCx → > 100,000 col of E. coli
Blood Cx → + E. coli

What would you do first?

Stabilize the patient.

1. IV antibiotics: Vancomycin, Gentamicin, Flagyl
2. Improve hemodynamics with IVF
3. Regulate glucose with insulin
4. Prepare for urgent surgical debridement

Would you obtain any imaging studies?

Obtain a CT abdomen/pelvis to evaluate for any pelvic/retroperitoneal gas/abscess.

CT abd/pelvis	→	(+) gas overlying scrotum, perineum, does not track in to the retroperitoneum, there appears to be a bone fragment piercing the rectum

What is your assessment?

Fournier's Gangrene with bone protruding into the rectum.

How would you treat this patient?

He needs surgical debridement as well as diverting colostomy and bone removal from the rectum. Obtain surgical consent and take him to the OR.

Discuss the procedure.

1. Dorsal lithotomy position
2. Wide debridement of the perineum and scrotum
3. Testicles left exposed
4. Have general surgery perform diverting colostomy
5. Insert presacral drains and bring out perineum
6. Pack the wound area with wet to dry dressings

Diverting colostomy has been performed and drains have been placed. The entire perineal area and scrotum has been debrided. The testicles are open to air.

How should the patient's wounds be managed?

1. Wound vac if possible is the best choice. It debrides the wound with changes and promotes granulation tissue, wound contraction, and decreases wound edema. It also decreases the need for daily dressing changes
2. Wet to dry dressing changes are an alternative. In reality, this often is what happens as wound vacs may not hold a good enough seal due to difficult perineal and thigh crease anatomy

You take the patient back to the OR 48 hours after the initial surgery for wound washout and debridement.

How should the testicles be managed?

Can consider placing them in thigh pouches if there is no remaining scrotal skin to close over the testicles.

The patient has completed a course of broad spectrum antibiotics and has been recovering well. His wounds show a nice bed of granulation tissue. He wants to be reconstructed.

What can you offer?

Scrotal and penile reconstruction can be offered using split thickness skin grafts. Grafts may be meshed or non-meshed. Reconstruction should be delayed until wounds are clean and free of infection.

CASE 5

HPI: 37-year-old male who presents to the ED with his wife. He developed penile pain during intercourse while his partner was on top of him. He heard a loud "pop" and noticed immediate detumescence and penile swelling. He has voided gross red blood once since the accident.

PMH: none

PSH: appendectomy

Allergies: none **Medications:** daily multi-vitamin

FH: non-contributory
SH: (-) tob; (+) ETOH socially
ROS: non-contributory

PE:

Vitals	T 98.8	BP 127/89	P 100	RR 14
General Exam	adult male; appears in moderate distress			
HEENT	benign			
Heart	normal sinus rhythm			
Lungs	CTA B			
Abdomen	soft, NTND			
Flank	(-) CVAT			
GU	(+) blood at the meatus; swollen and discolored phallus; testicles WNL; (-) butterfly ecchymosis of the perineum			
Prostate	small; anodular; not tender			
Ext	(-) CCE			
Neuro	non-focal; responds well to commands			

Labs:

Chem 7 → Cr 1.1, remainder WNL
CBC → WBC 11 K/µL, Hgb 12g/dL, HCT 38%
PT/PT → WNL

What is your assessment?

Penile fracture with urethral injury.

Would you obtain any imaging studies?

Yes, a retrograde urethrogram due to blood at the meatus. Men with penile fractures may also have an injured urethra. You should perform a RUG prior to catheter insertion. Alternatively, you may perform a RUG and/or cystoscopy in the OR at the time of exploration.

(+) extravasation of contrast in the mid pendulous urethra

What is the pathophysiology of penile fracture?

When the penis is erect, both corporal bodies are stretched to the limit of the tunica albuginea. In addition, the midline septum is also tightly stretched. When the penis buckles during intercourse, the result is a tear of the tunica albuginea.

Since the urethra is intimately associated with the corporal bodies, the tear in the tunica albuginea may also tear the spongiosum, thus causing a urethral injury. This mechanism of injury commonly occurs with the female partner straddling the male patient.

How would you treat this patient?

Immediate operative exploration with repair of the corporal bodies and the urethra.

Observation is a very poor choice in this scenario. The patient may develop impotence or severe penile curvature. Considering he also has a urethral injury, he could develop a corporal-urethral fistula.

Discuss the procedure.

Obtain operative consent for penile exploration, repair of penile fracture, urethral repair, cystoscopy and Foley catheter placement.

1. Perform cystoscopy, pass wire into bladder, place catheter over wire
2. Place occluding tourniquet at the base of the penis
3. Make a circumcising incision
4. Deglove the penis
5. Evacuate the hematoma
6. Identify the lacerated area of the urethra
   a. Dissect out lacerated urethra
   b. Excise devitalized tissue
   c. Close the urethral defect with water-tight closure using absorbable 4–0 or 5–0 suture. This should be done in a Heineke-Mikulicz fashion to preserve diameter of urethral lumen
   d. Close the tunica of the corpus spongiosum
7. Identify the lacerated area of the tunica albuginea
   a. Debride devitalized tunica tissues
   b. Close the tunica albuginea with absorbable suture
8. Close the skin

What is the follow up management?

Perform peri-catheter RUG in 14 days.

How do you manage penetrating trauma to the penis?

1. Penetrating injuries to the penis should be managed with operative exploration
2. Similar to the above described procedure, defects should be debrided and closed with absorbable suture
3. Urethral catheter or suprapubic tube drainage may be required depending on the location and severity of the injuries

How do you manage an amputated penis?

1. Clean the penis, wrap in sponge soaked with sterile saline and place in plastic zip lock bag
2. Keep the plastic bag in ice, and ensure the penis is not directly touching the ice
3. Reimplantation can be accomplished for as long as 18 hours from the time of amputation
4. Approximate the corporal bodies and urethra
5. Approximate the deep dorsal vein and artery
6. Approximate the nerve bundles

Note: Microvascular cavernosal artery approximation is not required.

How do you manage a degloving injury of the penis?

1. Remove all skin distal to the injury up to the corona of the glans (this skin will develop severe lymphedema if not removed due to the severed lymphatics)
2. Apply non-meshed STSG to the penile shaft and secure a bolster dressing over graft

CASE 6

HPI: You are consulted to the OB-GYN operating room for a urological complication. The patient is a 52-year-old female undergoing a transvaginal hysterectomy for uterine fibroids and bleeding. At the time of urethral catheter placement, the Foley balloon was noted to be in the vagina. On review of the chart it appears there is no prior urologic history.

PMH: renal insufficiency; DM; lower extremity neuropathy

PSH: C-section × 3

Allergies: none **Medications:** Insulin

FH: non-contributory
SH: (-) tob; (-) ETOH socially
ROS: non-contributory

PE:

Vitals	T 98.6	BP 120/40	P 100	RR 14
General Exam	middle aged F; intubated, sedated, and draped in dorsal lithotomy position			
HEENT	benign			
Abdomen	soft; not distended			
GU	normal external female genitalia; urethral catheter in urethral meatus with balloon visible in vaginal vault; pink mucosa is seen around the Foley balloon; bloody discharge in the field			

Labs:

Pre-operative labs include CBC, Chem 7, UA and UCx. All were WNL with exception of serum creatinine of 1.9 mL/dL.

What is your assessment?

Patient appears to have a bladder injury with communication to the vagina.

What would you do next?

You would assess the extent of the injury and rule out ureteral involvement.

Cystoscopy and IV indigo carmine or methylene blue
Or
Cystoscopy and retrograde pyelograms—this is the better option. It fully evaluates the upper tracts and even small injuries would be noted by extravasation of contrast. In addition if there is an injury, it provides anatomic detail to determine the level and extent of the injury, thus helping to determine the appropriate repair

The cystoscopy was difficult due to lack of bladder filling from the bladder injury. The right retrograde pyelogram was normal. The left demonstrated distal extravasation with no contrast making it into the proximal ureter.

What is your assessment?

Bladder injury with concomitant injury of the left ureter.

How would you proceed?

1. The patient needs an intraabdominal exploration to repair the injured ureter
   a. You should consent the next of kin
2. Open transabdominal repair of the bladder injury and left ureteral reimplant
   a. With distal ureteral injuries, reimplantation of the ureter into the bladder has the highest success rate
3. Re-prep and drape for an abdominal approach
4. Low midline or Pfannenstiel incision
5. Bivalve the bladder at dome
6. Explore the left ureter
7. Close the anterior vaginal wall
8. Close the bladder injury
9. Perform psoas hitch if necessary to perform tension free anastomosis
10. Reimplant the left ureter
    a. Place ureteral stent
11. Close the cystotomy
12. Place a pelvic drain

What is your post-operative care?

1. Remove pelvic drain when output is minimal; consider pelvic drain creatinine prior to removal to ensure no leak
2. Continue urethral catheter for 2 weeks, perform cystogram prior to removal
3. Continue ureteral stent for 4–6 weeks
4. No sexual activity for 4–6 weeks

The patient returns to clinic 1 week after urethral catheter removal complaining of constant incontinence. She has never had incontinence like this.

What is the differential diagnosis?

1. Vesicovaginal fistula
2. Ureterovaginal fistula
3. Both 1 & 2
4. New onset stress/urge incontinence

What is the next step?

Cystoscopy with bilateral RPG's and cystogram.

A punctate area of granulation tissue is noted at the bladder base. On cystogram there appears to be contrast in the vagina. Retrograde pyelograms are normal.

What is the next step?

Place a urethral catheter. Continue catheter for 2 weeks and have patient return for cystogram prior to removal of catheter.

The cystogram demonstrates persistent leakage from the base of the bladder to the vaginal vault. At this point the patient is 6 weeks out from the initial repair.

How would you manage this?

Plan for return to OR for vesicovaginal fistula repair via a transvaginal approach with interposition of peritoneal or Martius flap.

What is the blood supply to the Martius flap?

External pudendal artery to the anterior flap and internal pudendal artery to the posterior flap. You can sacrifice either supply depending on the positioning needs for the repair.

You perform a VVF repair with Martius flap interposition. The patient has a good result from the surgery.

How would you follow her long term considering the surgeries she has had?

Renal US and repeat serum Cr within 3–6 months to monitor for renal obstruction. Repeat renal US in 1 year.

CASE 7

HPI: 32-year-old Caucasian male with scrotal pain after being hit in the genitals with a hockey puck. Immediately after the injury he had intense pain and swelling in the scrotum and right testicle. He has voided since the incident without any gross hematuria. He relates he has no prior urologic history.

PMH: none

PSH: none

Allergies: none **Medications:** none

FH: non-contributory
SH: (-) tob; (-) ETOH socially
ROS: non-contributory

PE:

Vitals	T 98.6 BP 122/84 P 107 RR 15
General Exam	adult CM; appears in moderate distress
HEENT	benign
Heart	mild sinus tachycardia
Lungs	CTA B
Abdomen	soft; ND, NT
Flank	(-) CVAT
GU	circumcised; no lesions to the glans or shaft; left testicle descended; 20 g; no masses; right testicle very tender on exam, swollen; scrotum with ecchymosis
Prostate	small; anodular; not tender
Ext	(-) CCE
Neuro	non-focal; responds well to commands

Labs:

Chem 7 → Cr 0.8, remainder WNL
CBC → WBC 11 K/μL, Hgb 12g/dL, HCT 38%
PT/PT → WNL

What is your assessment?

Scrotal bruising versus testicular rupture.

What would you do first?

Scrotal US—has a high sensitivity to define ruptures of the tunica albuginea of the testicle.

The scrotal US demonstrates a hematocele with an abnormal appearance to the right testicle, but it is not definitive for a testicular rupture.

How do you manage this?

Proceed to OR for scrotal exploration.

Note: There is a high suspicion for testicular rupture in this case. The mechanism of injury and the physical exam finings all point to testicular rupture. Although scrotal US can detect a rupture, it can still be missed. Based on the exam and history, this patient should be explored.

Describe how you would explore this patient.

1. Urethral catheter
2. Midline scrotal incision
3. Dissect through dartos to right hemiscrotum
4. Evacuate hematoma
5. Identify the ruptured tunica
6. Trim back seminiferous tubules to allow primary closure of the tunica
7. Close tunica with fine absorbable suture (4–0 or 5–0)
8. Explore the contralateral side
9. Close dartos and skin in separate layers
10. Consider leaving a drain for 24–48 hours

He tolerates the procedure well and is discharged to home after 24 hours.

What is your follow up?

Return to clinic in 4 weeks for repeat exam. If the patient is doing well at that point, there is no indication for further imaging.

CHAPTER 19

URETHRAL STRICTURES

JAMES MASON, MD
LAWRENCE YEUNG, MD

CASE 1

HPI: You are consulted to the emergency department for a 27-year-old Caucasian male who presented with dysuria, frequency, and urinary urgency. The patient reports these symptoms have been present for about 2 days. Prior to that he noticed his stream becoming weaker for the past 3–4 months, and for the last 24 hours he has only been able to pass small drops of urine. He feels his bladder is very full and nothing gives relief. He denies other medical history, but admits to a remote history of sexually transmitted disease. The specifics of which he is unsure of, but he does remember receiving treatment at the local health department.

PMH: none

PSH: none

Allergies: none **Medications:** none

FH: (+) IDDM, (+) CAD
SH: (+) tob; (+) ETOH, social drinker
ROS: (+) dysuria; (+) urinary frequency; (-) flank pain

PE:

Vitals	T 99.2	BP 138/81	P 95	RR 14
GA	fully-developed, adult CM; appears stated age			
HEENT	benign			
Heart	slightly tachycardic; regular rate			
Lungs	breathing comfortably on room air			
Abdomen	suprapubic tenderness; patient guards on exam; no rebound			
Flank	(-) CVAT			
GU	normal circumcised male; patent meatus; bilateral testicles WNL			
Prostate	patient refuses			
Ext	(-) CCE			
Neuro	non-focal			

What additional history may be helpful?

American Urologic Association Symptom Score (AUASS). This is a 7-question survey designed to quantify symptoms related to BPH. Although our patient may be unlikely to have BPH, the AUASS provides a useful measure of obstructive related voiding symptoms.

AUASS:

0–7 = Mild Symptoms
8–19 = Moderate Symptoms
20–35 = Severe Symptoms

He reports AUASS of 22/35 (Severe Symptoms).

What laboratory and diagnostic testing would you obtain?

BMP → Cr 1.1, remainder normal
CBC → normal
UA → (-) nitrite, (small) leukocytes, 2 RBC

UCx → pending
Urine PCR for G/C → negative

What is the next step in evaluation?

Obtain Uroflow and post-void residual (PVR).

Uroflow → not available in emergency department
PVR → 475 mL

What is your assessment at this point?

The patient is in urinary retention.

What is your next step?

Place a urethral catheter.

You attempt to place a 16 F Foley, but meet resistance in the region of the bulbar urethra.

What is your next step?

After a failed catheter placement and existing history, the suspicion for urethral obstruction must be high. Considering the patient is <50 years old and has a prior history of STI, the obstruction is less likely related to benign prostatic hyperplasia. Within this age group, you must evaluate for urethral stricture or urethral foreign body.

What do you offer next?

Bedside cystoscopy. Be sure to obtain informed consent.

On cystoscopy there is a 5 French, thin bulbar urethral stricture. It appears very short (1–2 mm).

What are your options?

1. Urethral dilation over a wire
2. Urethral dilation with filiforms and followers
3. Suprapubic tube placement with future urethroplasty

You perform urethral dilation with filiforms and followers. The patient tolerates the procedure well. After dilation, you easily place a urethral catheter. The patient feels relieved and is discharged to home with the catheter.

The patient returns to your office in 3 days for urethral catheter removal.

He is able to void to completion after catheter removal. AUA guidelines state catheters may be removed within 72 hours of uncomplicated dilation or internal urethrotomy.

The patient returns to your office in 6 weeks for follow up.

You should perform a uroflow and PVR.

Uroflow → Qmax 24 mL/s
Voided Volume → 450 mL
PVR → 5 mL

His study is normal and he has no voiding complaints. He leaves your office happy.

5 years later, you are on call when the emergency room calls you about this same patient. He was involved in a high speed motor vehicle collision and had a trauma protocol CT head/chest/abdomen/pelvic that was significant only for a pelvic fracture. He has gross blood at his urethral meatus. He is hemodynamically stable, but has not been able to void since the accident.

What is your next step?

Perform a full physical exam.

1. Blood at the urethral meatus
2. DRE normal
3. Butterfly hematoma in perineum

What is the significance of the butterfly hematoma?

The classic presentation of a urethral injury contained within Colles' fascia is that of a butterfly hematoma of the perineum. Superiorly the extravasation can extend to the clavicles where Scarpa's fascia, the abdominal extension of Colles' fascia, attaches.

What is your next step?

Perform a retrograde urethrogram.

Shows complete obliteration on the urethra in the region of the membranous urethra. No contrast passes into the bladder.

What is your next step?

Place a suprapubic tube.

Describe how you would place an SPT.

1. Obtain informed consent
2. Palpate 2 finger breadths above pubic symphysis in the midline and anesthetize skin and intended SP tract
3. Identify bladder by aspiration with spinal needle and place SPT using kit that incorporates Seldinger technique over guidewire

   Note: while many other techniques are available, you should consider the safest technique possible for purposes of the oral exam.

SPT placed with return of 1000 mL of blood tinged urine.

What is your next step?

Because the patient is hemodynamically stable with only a pelvic fracture, you decide to take him to the OR for an attempt at endoscopic realignment of the urethra.

Describe how you would perform endoscopic realignment.

1. Obtain informed consent
2. Under general anesthesia and with 2 surgeons, flexible/rigid cystoscopy is performed simultaneously via the urethra and suprapubic tract to try to pass a wire across the defect; this can be done with the aid of fluoroscopy
3. Prolonged attempts at endoscopic realignment should not be performed as this can increase injury severity.

Unfortunately, you are unable to find the lumen of the distracted urethra to perform the realignment.

What is your next step?

Perform monthly SPT changes and then proceed with posterior urethroplasty in approximately 3 months.

Describe your approach to posterior urethral stricture repair.

1. Obtain informed consent
2. Standard or exaggerated lithotomy position
3. Lambda incision on the perineum
4. Divide bulbospongiosus muscle
5. Circumferentially mobilize urethra distally to penoscrotal junction and proximally to the obliterated segment of urethra
6. Excise intervening scar between distal urethral segment and apex of prostate
7. Identify prostatic apex

You find the apex of the prostate has been displaced in the cephalad position. Even after adequate distal mobilization of the urethra, it is still too short to reach the prostatic apex.

What do you do?

Separate the crura of the corpus cavernosa in the midline.

The urethra still does not reach. Now what?

Perform a pubectomy.

This gives you some additional length, but the distance remains too great to perform a tension free anastomosis.

What is the next option?

Re-route the urethra under one side of the corpus cavernosum.

After re-routing the urethra under the corpora, you are able to complete the anastomosis in a tension-free manner.

He sees you back in clinic in 2 weeks for a peri-catheter retrograde urethrogram, and no extravasation is seen so the catheter is removed. He thanks for you for your help.

CASE 2

HPI: 51-year-old Caucasian male with severe LUTS presents to your office. He first noticed his symptoms 3 months ago and they have been stable for the last 4 weeks. He recalls a straddle injury while climbing over a fence about 5 years ago. He had a history of prior urethral "cutting" procedure by a formal local urologist. He has a history of a ureteral stone requiring ureteral stent and SWL > 10 years ago.

PMH: HTN; HLD

PSH: Appendectomy as adolescent

Allergies: NKDA **Medications:** none

FH: (+) HTN; (+) DM
SH: (-) tob; (-) ETOH
ROS: (+) urinary frequency; (+) urinary urgency; (+) weak stream

PE:

Vitals	T 99.8	BP 124/80	P 78	RR 12
GA	fully-developed, well-groomed adult CM			
HEENT	benign			
Heart	RRR			
Lungs	breathing comfortably on room air			
Abdomen	soft; non tender; no guarding; low midline fullness			
Flank	(-) CVAT			
GU	normal circumcised male; patent meatus; no lesions; testicles without masses			
Prostate	30 g; smooth; (-) nodules or induration			
Ext	(-) CCE			
Neuro	non-focal			

What laboratory and diagnostic testing would you obtain?

BMP → normal
CBC → normal
UA → (-) nitrite, (-) leukocytes, (-) RBC
UCx → pending

What additional history may be helpful in evaluation?

You should question the patient about any history (remote or recent) of sexually transmitted diseases. Further detailed history regarding his prior stone history and the specifics of his procedure may be helpful.

Additionally, obtaining an AUA symptom score to help clarify the degree of bother with his urinary symptoms may help when trying to determine what initial therapies to start and to determine the response on future visits.

AUA symptom score is 33 (severe LUTS).

What is the next step in evaluation?

Obtain Uroflow and post-void residual (PVR).

Uroflow → Qmax 3 cc/sec: (long plateau curve)
Voided Volume → 150 mL
PVR → 325 mL

What is your assessment at this point?

He has an obstructed flow rate. His PVR is elevated. Etiologies can include neurogenic bladder, benign prostatic hyperplasia, or urethral stricture recurrence.

What is your next step?

Considering the rapid onset of symptoms with prior history of urethral stricture, cystoscopy with possible retrograde urethrography should be offered to evaluate for urethral stricture or prostatic obstruction.

On cystoscopy there is a pinpoint (5 F) bulbar urethral stricture.

What is your next step?

Determine stricture length. You should perform retrograde urethrography to determine length and location of the stricture as this will guide your management options.

You find he has a 2 cm mid bulbar urethral stricture.

What are your treatment options?

He needs an open urethroplasty. For bulbar strictures ≥2 cm you should offer urethroplasty as initial treatment option given the low success rates of DVIU or dilation (AUA guideline).

Additionally, AUA guidelines state that urethroplasty should be performed as opposed to repeat endoscopic management after failed dilation or DVIU due to low retreatment success rates.

You discuss performing a urethroplasty. Based on the length of the stricture, you anticipate that you should be able to perform an excision and primary anastomotic (EPA) urethroplasty.

How do you proceed?

Obtain informed consent and preoperative labs. Counsel the patient on perioperative risk of the procedure including: bleeding, infection, stricture recurrence, erectile dysfunction, ejaculatory dysfunction, urethrocutaneous fistula formation, penile chordee, altered penile sensation, and post void dribbling. Give peri-operative antibiotics.

Discuss the surgical principles of an EPA urethroplasty.

1. Make a vertical midline perineal skin incision
2. Dissect through Colles' fascia

3. Divide the bulbospongiosus muscle
4. Circumferentially mobilize the urethra distally to the penoscrotal junction and proximally toward the membranous urethra after dividing the central tendon
5. Identify level of stricture by cystourethroscopy
6. Excise the urethral stricture
7. Spatulate proximal and distal ends of the urethra 1 cm on each side
    a. Distal side—spatulate ventrally
    b. Proximal side—spatulate dorsally as the bulbospongiosus tissue is thicker ventrally as you go proximally
8. Perform the anastomosis with interrupted absorbable suture
9. Insert Foley catheter
10. Close the incision

He tolerates the procedure well and is discharged to home post-operatively. He returns for peri-catheter retrograde urethrogram and voiding trial in 2 weeks. This is successful. He returns for follow up every 3 months for the first year with Uroflow and PVR for surveillance for stricture recurrence.

He returns 6 months after his EPA with worsening LUTS and a weak urine stream. A RUG is performed in the clinic, which shows a 4 cm mid bulbar urethral stricture with a narrow lumen.

Discuss your surgical approach for this mid bulbar stricture.

Considering length of the stricture, you discuss tissue substitution urethroplasty. AUA Guidelines state oral mucosa grafts should be considered before other grafts or flaps when tissue substitution is required.

You decide that an augmented anastomotic buccal mucosa graft urethroplasty is the best option considering he has a long stricture with a narrow lumen.

Describe the surgical technique for an augmented anastomotic dorsal buccal mucosa graft urethroplasty.

1. Make a vertical midline perineal skin incision
2. Dissect through Colles' fascia
3. Sharply divide the bulbospongiosus muscle
4. Identify level of stricture by cystourethroscopy
5. Excise the urethral stricture
6. Spatulate urethra dorsally 1 cm on each end. Measure defect distance
7. Harvest buccal mucosa graft to cover measured urethral defect
8. Fenestrate buccal graft (only for dorsal onlay—do not fenestrate if placing ventral)
9. Lay graft on corporal bodies and secure with absorbable suture
10. Close lateral sides of buccal graft to native urethra with absorbable suture
11. Test anastomosis for water tightness by instilling irrigation into urethra
12. Insert urethral catheter
13. Close the incision

He recovers well from the operation and is discharged home post-operatively. He returns 5 years later with recurrent voiding problems. His stream is now very weak. Uroflow is concerning for stricture recurrence. Cystoscopy and retrograde urethrogram confirm a long penile urethral stricture (6 cm). There is no evidence of Lichen Sclerosus et Atrophicus (LSA) on genital exam.

What do you recommend?

Recommend pedicle vertical penile skin flap (Orandi flap). Use of genital skin in the presence of LSA is associated with increased failure rates.

Discuss the surgical technique for the Orandi flap.

1. Mark a long hexagonal flap adjacent to the strictured portion of the urethra, approximating the length of the stricture
2. Incise the long vertical segment of the flap closest to the urethra superficially down to, but not through, the dartos pedicle
3. Incise the long vertical segment furthest from the urethra through the dartos fascia down to Buck's fascia. This will serve as the deep incision
4. Dissect on top of Buck's fascia back toward the urethra to mobilize the pedicle
5. Blood supply of the pedicle is based on dartos fascia
6. Make a urethrotomy to open up the entire length of the stricture until healthy urethra is exposed
7. Invert the pedicle flap to approximate the epithelial edges and the urethral mucosa with absorbable suture
8. Insert Foley catheter
9. Close the incision

The operation was successful. However, he returns 1 year later with severe LUTS. Cystoscopy and RUG demonstrates a panurethral stricture. He has no redundant penile skin left to use for urethroplasty.

What do you recommend next?

Staged graft urethroplasty (Schreiter) or perineal urethrostomy.

Patient elects staged urethroplasty.

Discuss your surgical technique for the staged urethroplasty.

1. Incise urethra ventrally full thickness through to the penile skin until normal caliber urethra is exposed
2. Run open edge of corpus spongiosum tissue closed for hemostasis
3. Mobilize the dartos tissue to the edges of the urethral plate and secure to plate
4. Measure length of urethral segment to be segmented with graft
5. Harvest buccal mucosa. If insufficient buccal mucosa available, then harvest split thickness skin graft from anterior thigh
6. Suture the graft to dartos tissue on both sides of the opened urethral plate
7. Place bolster dressing on graft site for 5 days before removing
8. Bring the patient back to the OR when the graft is supple to tubularize (minimum of 6 months)
9. Outline a 3 cm wide epithelial strip to create a 30F neourethra. Incise flap down to dartos
10. Approximate the epithelial edges to complete the neourethra using absorbable suture
11. Insert Foley catheter
12. Close the incision

Describe complications of urethroplasty surgery.

1. Recurrent urethral stricture
2. Urethrocutaneous fistula

3. Erectile dysfunction
4. Ejaculatory dysfunction
5. Post void dribbling
6. Change in penile sensation
7. Urethral bezoar (with use of hair bearing skin for graft)

What is the blood supply to the penile skin?

1. Superficial blood supply
    a. Subdermal plexus connects to intradermal plexus via dermal perforators
2. Deep blood supply
    a. Vascular plexus of Buck's and dartos fascia

What is the blood supply to the penis?

1. Internal iliac artery
2. Internal pudendal artery
3. Common penile artery
    a. Bulbourethral artery → corpus spongiosum
    b. Dorsal artery of the penis → glans penis
    c. Cavernosal artery → corpus cavernosa
    d. Circumflex arteries → crus of corpus cavernosa

What is the blood supply to the urethra?

The urethra has a dual blood supply.

1. Proximal blood supply
    a. Bulbourethral artery → proximal corpus spongiosum
2. Distal blood supply
    a. Dorsal artery of penis → via communicators to glans penis

Note: The male urethra can survive mobilization on either end as a result of this dual blood supply. Caution must be exercised when there is a prior history of urethral disease, surgery or trauma. History of prior hypospadias repair (distal blood supply is absent due to congenitally deficient spongiosum tissue) or pelvic trauma (proximal blood supply may be disrupted) may mean a single blood supply to the urethra. Mobilization of the urethra in these circumstances may result in tissue ischemia, necrosis, or recurrent stricture.

Discuss the Algorithm for Bulbar Urethral Stricture.

History & Physical
↓
1. Retrograde Urethrogram + VCUG
2. Urethroscopy
↓
<2 cm → Urethral dilation or DVIU or urethroplasty
≥2 cm or prior Dilation/DVIU → urethroplasty
Limit attempts at dilation or DVIU to 1 attempt.

Discuss the Algorithm for Penile Urethral Stricture.

History & Physical

↓

1. Retrograde Urethrogram + VCUG
2. Urethroscopy

↓

Urethroplasty

Types of Urethroplasty:

1. Excision and Primary Anastomosis (EPA)
    - Applicable location: bulbar, membranous urethra
    - Applicable stricture length: 1–3 cm

    Note: Avoid with longer strictures to avoid high tension anastomosis. Caution when approaching penoscrotal junction as can cause penile chordee. Good spatulation (~1 cm) on each end gives best chance at widely patent anastomosis. Be sure to include spatulation in calculation for distance needed to span defect (e.g., 1 cm stricture excision + 1 cm distal spatulation + 1 cm proximal spatulation = 3 cm defect).

    See prior operative description

2. Dorsal onlay buccal graft urethroplasty (Barbagli)
    - Applicable location: penile, bulbar
    - Applicable stricture length: typically reserved for longer strictures (i.e., > 3 cm) with at least 1 cm native urethral plate to augment

    Note: Use non-hair bearing skin (oral mucosa, foreskin, penile shaft, split thickness skin graft). Be sure to properly spread fix graft to corporal bodies.

    a. Mobilize urethra off corporal bodies and rotate
    b. Make dorsal urethrotomy through stricture and carry 1 cm distally and proximally to normal urethral lumen
    c. Spread fix and quilt graft to corporal bodies
    d. Reapproximate edges of urethra to graft edges
3. Ventral onlay graft urethroplasty
    - Applicable location: typically proximal bulbar urethra
    - Applicable stricture length: typically reserved for longer strictures (i.e., >3 cm) with at least 1 cm native urethral plate to augment

    Note: Use non-hair bearing skin (oral mucosa, foreskin, penile shaft, split thickness skin graft). Best used in the proximal bulbar urethra due to added graft support from the thicker ventral corpus spongiosum.

    a. Incise urethra vertically through stricture and carry 1 cm distally and proximally to normal urethral lumen
    b. Approximate edges of opened urethra to the edges of the graft
    c. Place urethral catheter
    d. Close ventral corpus spongiosum over graft
4. Dorsal inlay graft urethroplasty (Asopa)
    - Applicable location: penile urethra
    - Stricture length applicable: limited to amount of oral mucosa available for graft

    Note: Use oral mucosal graft.

    a. Perform ventral urethrotomy along length of stricture and 1 cm into proximal and distal segments of normal urethra
    b. Incise dorsal surface of urethra along stricture

   c. Lay down harvested oral mucosa. Fix to edges of urethra and quilt to corporal bodies
   d. Close ventral corpus spongiosum
   e. Place urethral catheter
   f. Close skin

5. Augmented Anastomotic Urethroplasty
   - Applicable location: bulbar urethra
   - Applicable stricture length: >2–3 cm (when EPA will not work)

   Note: Used for long, very narrow lumen strictures. Excise stricture and scar tissue.

   See prior operative description

6. Pedicle Flap Urethroplasty
   - Applicable location: penile, bulbar
   - Applicable stricture length: >2–3 cm (when EPA will not work)

   Note: Avoid penile skin use in the presence of lichen sclerosis. Preservation of supple dartos pedicle is paramount for survival of flap. Caution in patients with limited redundant penile skin or prior penile skin harvest, as overly aggressive harvest may cause cosmetic or functional penile defects

   a. Transverse island flap (Duckett)
      i. Created from transverse penile shaft skin based on dartos pedicle
      ii. Incise the urethra vertically and sew in the pedicle flap
   b. Vertical flap (Orandi)
      i. Created from longitudinal penile shaft skin based on dartos pedicle
      ii. Incise the urethra vertically and sew in the pedicle flap
   c. Transverse circular penile skin flap (McAninch)
      i. Flap created from 2 cm wide segment of inner preputial (uncircumcised) or distal penile skin (circumcised) and is based on dartos pedicle
      ii. Incise the urethra vertically and sew in the pedicle flap

7. Staged urethroplasty
   - Applicable location: penile, bulbar
   - Applicable stricture length: for long, recurrent urethral strictures

   Note: Allow first stage to mature 6–12 months for adequate neovascularization of the tissue to be tubularized. Form a 30 French urethral tube (approximately 3 cm wide to account for 20% skin contracture, leaving approximately 24F urethra after graft contracture) over appropriate sized catheter.

   a. Johanson urethroplasty
      i. Perform ventral stricturotomy
      ii. Approximate penile/scrotal skin to either side of dorsal urethral plate
      iii. Allow to heal and develop neovascularity (minimum 3–6 months
      iv. Tubularize neourethral plate (approximately 3 cm wide to result in 24F urethra after contracture)
      v. Close skin over urethra
   b. Staged graft urethroplasty (Schreiter)
      i. Perform ventral stricturotomy
      ii. Sew down split thickness graft or buccal mucosa to one or both sides of dorsal urethral plate and to penile skin edges
      iii. Allow epithelialization and neovascularity (minimum of 6 months)
      iv. Tubularize neourethral plate (approximately 3 cm wide to result in 24F urethra after contracture)
      v. Close skin over urethra

Lawrence L. Yeung, MD is an assistant professor and director of male reconstructive urology, incontinence, and erectile dysfunction in the Department of Urology at the University of Florida College of Medicine. He attended medical school and was a resident in urology at the same institution. In addition, he completed a fellowship in reconstructive urology at Washington University in St. Louis.

Dr. Yeung's clinical interests include reconstructive surgery of the genitals and urinary tract to correct defects resulting from trauma, cancer, infections and other causes. Among the journals in which Dr. Yeung has published articles are: Advances in Urology; Case Reports in Urology; Journal of Surgical Education; Journal of Urology; and Urology.

Editor

Lawrence L. Yeung, MD
Assistant Professor
Genitourinary Reconstruction
Department of Urology, University of Florida
Gainesville, FL

Choe's Urology Contributors

Jeremy Bergamo, MD
Department of Urology, University of Florida
Gainesville, FL

Aaron Brafman, MD
Department of Urology, University of Florida
Gainesville, FL

Peter Cai, MD
Department of Urology
Weill Cornell Medicine
New York, NY

Benjamin K. Canales, MD, MPH
Associate Professor
Department of Urology, University of Florida
Gainesville, FL

Bilal I. Chughtai, MD
Assistant Professor of Urology
Assistant Professor of Urology in Obstetrics and Gynecology
Weill Cornell Medicine
New York, NY

Paul L. Crispen, MD
Associate Professor
Department of Urology, University of Florida
Gainesville, FL

Romano T. DeMarco, MD
Associate Professor
Chief, Division of Pediatric Urology
Department of Urology, University of Florida
Gainesville, FL

Gregory J. Diorio, DO
Department of Genitourinary Oncology
H. Lee Moffitt Cancer Center and Research Institute
Tampa, FL

Scott M. Gilbert, MD
Associate Member
Department of Genitourinary Oncology
H. Lee Moffitt Cancer Center and Research Institute
Tampa, FL

Mohit Gupta, MD
Department of Urology, University of Florida
Gainesville, FL

Julia Han, MD
Department of Urology, University of Florida
Gainesville, FL

Samay Jain, MD
Assistant Professor
Chief, Division of Urologic Oncology
Medical Director, Urology Clinic
Interim Associate Chief Medical Officer
Department of Urology, University of Toledo
Toledo, OH

Nikki P. Le, MD
Urology Austin
Austin, TX

Andrew R. Leone, MD
Department of Genitourinary Oncology
H. Lee Moffitt Cancer Center and Research Institute
Tampa, FL

James Bradley Mason, MD
Department of Urology, University of Florida
Gainesville, FL

John P. Mulhall, MD, MSc, FECSM, FACS
Director of Sexual & Reproductive Medicine
Urology Service, Department of Surgery
Memorial Sloan Kettering Cancer Center

Bobby B. Najari, MD
Assistant Professor, Department of Urology
NYU Langone Medical Center
New York, NY

Brandon Otto, MD
Assistant Professor
Department of Urology, University of Florida
Gainesville, FL

Sijo J. Parekattil, MD
Co-Director The Personalized Urology & Robotics Clinic
Clermont, FL

Jonathan Pavlinec, MD
Department of Urology, University of Florida
Gainesville, FL

Edward N. Rampersaud, MD
Assistant Professor of Surgery
Urologic Oncology
Duke Cancer Institute
Duke University School of Medicine

Philippe E. Spiess, MD
Associate Member
Department of Genitourinary Oncology H. Lee Moffitt Cancer Center and Research Institute
Tampa, FL

Dominique Thomas, BS
Weill Cornell Medicine
Department of Urology
New York, NY

Marla Wardenburg, MD
Department of Urology, University of Florida
Gainesville, FL

Akira Yamamoto, MD
Department of Urology, University of Florida
Gainesville, FL

Uwais B. Zaid, MD
Genitourinary Reconstruction and Female Urology
Carle Foundation Hospital
Department of Urology
Champaign, Il

Anja Zann, MD
Department of Urology, University of Florida
Gainesville, FL

ISBN 978-1-890018-80-1
90000>
9 781890 018801

Anadem Publishing
3620 North High Street • Columbus, OH 43214
1-800-633-0055 • 614-262-2539 • Fax: 614-262-6630
anadem@anadem.com • www.anadem.com